UGSF - Unité de Glycobiologie Structurale et Fonctionnelle

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Unité de Glycobiologie Structurale et Fonctionnelle

UGSF

Under the supervision of the following institutions and research bodies:

Centre National de la Recherche Scientifique - CNRS

Université Lille 1 – Sciences et Technologies - USTL

December 2013

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

Department for the evaluation of research units

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

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

On behalf of the expert committee,

- MS Anne IMBERTY, chair of the committee

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

Evaluation report

This report is the result of the evaluation by the experts committee, the composition of which is specified below. The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Unité de Glycobiologie Structurale et Fonctionnelle
Unit acronym:	UGSF
Label requested:	UMR
Present no:	UMR 8576
Name of Director (2013-2014):	Mr Christophe D'HULST
Name of Project Leader (2015-2019):	Mr Christophe D'HULST

Expert committee members

Chair:	Ms Anne IMBERTY, Centre national de la recherche scientifique, Grenoble
Experts:	Mr Markus AEBI, ETH Zurich, Switzerland
	Mr Henrik CLAUSEN, University of Copenhagen, Denmark
	Ms Cristina DE CASTRO, University of Napoli, Italy
	Ms Rita GERARDY-SCHAHN, University of Hannover, Germany
	Mr Patrice LEROUGE, University of Rouen
	Mr Hugues LORTAT-JACOB (representative of CoCNRS), University of Grenoble
	Ms Catherine RONIN, University of Aix-Marseille
	Mr Marc SAVASTA, University of Grenoble
	Mr Jean-Marie SCHMITTER, University of Bordeaux
	Ms Jean-Pierre SIMORRE, University of Grenoble
	Ms Birte SVENSSON, University Polytechnic of Lyngby, Denmark

Scientific delegate representing the AERES:

Ms Sophie De BENTZMANN

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

Ms Florence NOBLE (Centre national de la recherche scientifique)

Mr Jean-François PAUWELS (University Lille 1 – Science and Technology - USTL)

Mr Philippe DELANNOY (Representative of Doctoral School 446)

1 • Introduction

History and geographical location of the unit

The research unit "Glycobiologie Structurale et Fonctionnelle (UGSF)" has been founded more than 30 years ago. The research teams are located in one building in the campus of University Lille 1, Sciences and Technologies located in Villeneuve d'Ascq. The original building was extended in 1994 and a recent refurbishment of the basement brought some additional spaces for meeting rooms and other facilities. The 900 MHz NMR spectrometer, which belongs to a national infrastructure network (Très Grande Infrastructure de Recherche), is located in a new building in the nearby site of "Haute Borne". The research unit is part of the local Federation de Recherche IFR147 that will become "Fédération de Recherche" Structural and Functional Biochemistry of Biomolecular Assemblies.

Management team

The former director, Mr Jean-Claude MICHALSKI, accepted the invitation to join the direction team of the Life Science Department of the Head Quarter of CNRS in 2013. Mr Christophe D'HULST was elected as the acting director for the period 1st March 2013 to 31st August 2013. He was appointed as the director on 1st September 2013 to complete the present mandate up to 2014 with the responsibility to set up the strategy plan for the next coming period (2015-2020). He was assisted by Mr Jean-Claude MICHALSKI as Deputy director until January 2014 and then by Mr Yann GUERARDEL.

AERES nomenclature

SVE1_LS1 Biologie Moléculare et Structurale, Biochimie

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	37	48
N2: Permanent researchers from Institutions and similar positions	14	13
N3: Other permanent staff (without research duties)	24	25
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	2	
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	6	1
N6: Other contractual staff (without research duties)	13	3
TOTAL N1 to N6	**96**	**90**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	22	
Theses defended	37	
Postdoctoral students having spent at least 12 months in the unit*	18	
Number of Research Supervisor Qualifications (HDR) taken	12	
Qualified research supervisors (with an HDR) or similar positions	39	43

2 • Assessment of the unit

Overall opinion about the unit

The activities of the research unit are centered on the "Glycobiology" domain which encompasses the study of the structure, biosynthesis, and biology of glycans with the aim of unravelling the relationship between their structures ans their functions. This is the largest European research unit in the field of Glycobiology. Internationally, it is among the top three centers that focus on the role of glycans in living organisms and on the applications in medical, biochemical and biotechnological fields. The past directors were highly recognized internationally and they have been able to give a strong scientific identity to this department.

The unit consists of 10 research teams that are organized in three axes: 1. Structure, 2. Biosynthesis, degradation, regulation and 3. Function, pathologies. In-house facilities include classic technical services and one platform dedicated to structural analysis of glycoconjugates (PAGés). Larger facilities are available at the level of the university with access to NMR, mass spectrometry, cellular imaging, green and animal houses.

As a global view, the committee has appreciated the association between a strong know-how in glycosciences and a multidisciplinary approach. The dynamism of the new generation of team leaders has been also noted. The project is well balanced since it is based on solid existing research but also proposes a new structuration with emergence of young teams and integration of an external group that will reinforce the research in plant science. With the appropriate investment in technology upgrade and international training, the research unit has all the potential for becoming the reference department in glycan analysis for european research laboratories and companies.

Strengths and opportunities related to the context

Glycans have inherent complexity and the research teams of UGSF have developed and continue to develop unique skills in a scientifically and technically difficult area. Such an endeavour along with an excellent reputation at the national and international levels provides the basis for conducting cutting edge research. This position offers the possibility to actively participate in the shaping of glycoscience at an international level. Taking leading roles in european networks and organizing international workshops, meetings and schools can be examples of such activities.

While centered on one class of biomolecules, the researchers have been able to assemble a very wide spectrum of experimental approaches and biological models, including microbes, algae, plants, animals and patients. Equilibrium between high profitable diversity and more risky dispersion has to be maintained. The recent inclusion of synthetic chemists with strong expertise in chemical biology approaches is likely to provide an asset to face new challenges in cellular biology. Similarly, the recruitement of a researcher with expertise in cristallography has reinforced the structural biology approach. The variety of biological models along with the accumulation of data obtained from the different approaches provide excellent opportunities for entering into the "omics" millennium. Several teams of the department have already started to use genomics or phylogenetic tools in their research. This will provide a significant move towards the integration of novel scientific and technology tools which are not used at their full potential at the present time.

Over its history, the research unit has created and maintained strong links with university throughout a dedicated and major involvement in teaching and training actions. The research unit benefited from a regular recruitment of assistant professors, including one in 2014 for supporting the high field NMR activity. The high percentage of young scientists in the research teams results in a very dynamic atmosphere. It favors the emergence of young and energetic leaders who are rapidly gaining international recognition.

Weaknesses and threats related to the context

In the future period, the research unit will be composed of 12 research teams directed by competent and productive, and mostly young researchers. While they have the full possibility to develop their research at UGSF, it will be necessary to provide actions for maintaining the scientific cohesion.

The excellent expertise in the domain of glycosciences offers many opportunities to be part of research networks and grant applications. Nevertheless, this should not deter the scientists from being ambitious enough to push their own research in the front line by initiating and coordinating national and european networks and competing at the highest level for prestigious grants.

Recommendations

The emergence of a new generation of young scientists as group leaders should provide the required momentum for new perspectives in glycosciences. The scientific cohesion of the research unit should benefit from convergent interdiscplinary activities such as the organization of international training platfom dedicated to glycosciences, for example. This potential attractiveness can also be encouraged by developing and extending the analytical platforms. The research unit should clearly position itself as the reference laboratory for structural analysis in glycosciences not only for european research laboratories, but also for pharmaceutical or food science companies that have a strong demand in this area.

The biological projects are now well balanced between models related to animal science and those related to plant science. This latter field will benefit from the arrival of a new team specialized in plant cell walls. Microbiology is also present although it appears dispersed in different sub-projects around several teams. The team “Génétique des enveloppes bactériennes” has a subcritical size and this axis may be reinforced, eventually through attracting microbiologists or merging with another team with international recognition.

The search for novel and international funding for high quality science should become of a crucial importance in the coming years. The present financial income of the research unit is not very high, with respect to the number of researchers. The decrease of institutional funding associated with lower chance of success at the National funding Agency (ANR) may threaten the economy of the research if there are no counteracting measures. The concurrent loss of positions of technical staff will also have to be compensated by increasing financial income from contracts.

3 • Detailed assessments

Assessment of scientific quality and outputs

The strong point of the research unit lies in its capacity of covering most aspects of glycobiology. This expertise covers the field of structural analysis of glycans in microbes, plants or animal models, as well as the biosynthesis of glycoconjugates and their regulation, and their implications in biological functions and related diseases. Scientific breakthroughs resulting in highly visible results have been obtained in areas such as starch metabolism and related evolution, glycosylation mechanisms and phylogeny of related enzymes, molecular mechanism of cell signaling and of glycosylation disorders and genome sequence, structural biology of neurodegenerative diseases and epigenetics of prenatal stress.

The scientific production is excellent with more than 330 publications in the reference period (2008 to mid 2013). A steady increase in the number of publications has been observed during this period reaching more than 65 publications in 2011 and 2012 (approx. 1.3 publications per researcher per year). 42% of the articles have been published in journals with impact factor greater than 4 and 18 articles greater than 10. An active involvement in consortia devoted to new genomes sequencing resulted in very high impact articles published in Nature and Science. The publications of some articles in excellent general journals such as PNAS has to be acknowledged. The domain of publication is very wide covering the field of chemistry, structural biology, biochemistry, molecular biology, plant biochemistry, plant physiology, enzymology, neurosciences. In all of these domains, the researchers demonstrated their capacity to push glycosciences at the top level and to publish in the best journals of each speciality (Angew. Chem., J. Amer. Chem. Soc., Plant Cell, Human Genetics, Mol Cell. Proteom., Hepatology, J. Neurosci…). It is recognized that about 15% of the published articles result from in-house collaborations.

Assessment of the unit's academic reputation

The research unit has an excellent reputation at the national level for its successful interface between chemistry and biology. Scientific symposia including the French Glycosciences meeting in 2012 have been organized under direction of the members of the research unit. The availability of top equipment, such as the 900 MHz NMR, as part of the CNRS very large instrument network, is also a tool for attractiveness. The large number of review papers and the numerous invitations to conferences and seminars (more than 150) acknowledge the excellent scientific recognition of the researchers. The recognition at the national level is also attested by the strong participation of the researchers in commissions and evaluation committees (five sections of CoNRS). Some of the young researchers have already reached national recognition with awards of two bronze medals from CNRS as well as international recognition with invitations to Gordon conferences.

At the international level, the research unit offers unique expertise in Europe, resulting in a high level of visibility and attractiveness that has to be maintained and reinforced in the future. Several highly recognized scientists performed sabbatical stay in the research unit. Some of the researchers are involved in international networks on genome sequencing or diseases, and several bilateral collaborations have been established with Portugal, Taiwan, Mexico, Japan…. In the field of neurosciences, an international laboratory (Laboratoire International Associé) has been created with Sapienza university in Rome.

The active participation in local, national and international networks has been the basis for obtaining funds from competitive calls. During the 5 years period, the research unit coordinated 8 ANR grants and participated in 10 others. In the National Excellence initiative, UGSF is involved in one LABEX (Distals) and one IEED IFMAS. Involvement in health-related subjects also brings grants from several charity foundations related to pathologies such as Cancer and Cystic fibrosis. At the European levels, the research unit is involved in two EU Marie-Curie networks.

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

Some of the teams are involved in translational research activity thanks to their unique expertise in analysis of glycoconjugates and to their understanding of the complexity of glycosylation mechanisms. Eight patents have been deposited since 2008. Historically, the research unit was mostly collaborating with the local agro-food companies Roquette Frères and Lesaffre. The activity of the INRA-associated team on chemical communication is of direct interest to animal farming companies and new products are being developed. More recently, research contracts were established with biopharmaceutical national companies (Endotis-Pharma, LFB, Institut Pierre Fabre, Servier…) and international ones (Tate and Tyle, Vitamed..).

The industrial partnership provides about 10% for the funding of the UGSF (excluding permanent staff salaries). Taking into account the available instrumental platform and the unique expertise in structural analysis of glycans that is of high demand in pharmaceutical industry, it should be expected that more funding could be obtained from such sources, helping in securing the financial income of the research unit.

Assessment of the unit's organisation and life

The managing team is composed of the director and the deputy-director. They are advised by the management board consisting of all team leaders and by the laboratory council that meets 3-4 times per year. The administrative and technical services are all well organized. Most of the technical staff shares its time between participation to common services and participation to team projects, an organization that allows them to be involved directly in science. Because of the departure of seven technical staff in the last period, some of the technical services are endangered, which increases the burden of technical work for young researchers. The creation of the PAGès platform which is a spin-off the "biodiversity associated with glycoconjugates" team is an excellent move towards technological transfer. Its should progressively become more independent and attracts contracts from other laboratories and from companies.

The research unit is divided into 10 teams (12 in the next period) and efforts have been made in order to maintain scientific communication and cohesion between researchers. The organization of a weekly seminar, with topics selected by each team in turn, as well as the organisation of an annual 2-days general retreat are positive actions. Development of appropriate computer tools for sharing administrative and scientific information would be beneficial.

Involvement in training through research

The research unit has a very close relationship with university Lille 1 since most of the researchers have a professorship or assistant professorship position directly involved with educational tasks. At the Bachelor level (Licence), members of the unit are in charge of modules in the speciality of Biology, Biology and Biotechnology and Life Sciences. At the Master level, staff are in charge of the "Structural and Molecular Biology" option of the Master in Biology and Biotechnology. Other researchers are responsible for Masters in different areas such as food and nutrition, biology and health (both common to universities Lille 1 and Lille 2) and Chemistry and Biology (University Lille 1). An international Master in Plant Sciences will be created in 2015 under the direction of a new team. The doctoral school "Biology and Heath" that counts more than 300 graduate students is also co-directed by a member of the research unit.

The unit is hosting 28 PhD students of this doctoral school, with approximately 8 new students per year. Involvement in training through research is also visible as indicated by the high number of students trained in the laboratory during the two years of the master course programme (more than 20 each year), as well as trainees for other academic degrees.

In addition, some teams have been involved in a national workshop, such as CNRS training in high field NMR. Such initiatives could be extended to other expertises present in the research unit throughout the organisation of international training schools in glycosciences that would be of high interest to many teams in Europe.

Assessment of the strategy and the five-year plan

The scientific project is excellent as it is founded on the high quality of the existing research while proposing the emergence of new team leaders and the inclusion of external teams. Two emergent teams will result from the splitting of one large group. The young researchers who will be in charge have international recognition and the ability to attract fundings. The arrival of a local research group working on plant cell walls from flax should reinforce the plant science axis of the research unit. Besides, this team has very good scientific production and strong translational research activity. Finally, the team on "Olfaction of Glycobiology" that was hosted in the research unit, just obtained association with INRA. This team is also involved in translational research and its association with INRA should provide an opportunity to reinforce its human potential, that is subcritical at the present time.

The new project involves a reorganisation in three sections according to their respective approaches: “molecular approaches”, “cellular approaches” and “integrated approaches”. It is recommended to associate some scientific animation to each of these axes in order to enforce some cohesion. It has to be noted that not all teams have reached the same level of excellence and such a reorganisation should take into account the reinforcing or integration of the more fragile teams. Inter-team collaborations and synergy should be reinforced in order to pull all the teams at the excellence levels already reached by some of them. The strength of the research unit resides more in its strong originality and visibility in the French and European scientific landscape than in the excellence of some of the teams.

4 • Team by team analysis

Team 1: Biodiversity associated to glycoconjugates

Name of team leader: Mr Yann GUERARDEL

Workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	7	9
N2: Permanent researchers from Institutions and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**10**	**11**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit*	3	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	6	6

• Detailed assessments

The team "Biodiversity associated to glycoconjugates" focuses its research on characterizing the glycosylation of micro-organisms and their hosts, with developments in the area of therapeutic agents and analysis tools. The structural elucidation of carbohydrate-containing compounds from different microorganisms (Mycobacterium marinum, Candida albicans, Bacillus species and Escherichia coli) is performed with appropriate structure-function studies and also aims at unraveling of the biosynthetic processes behind. The glycosylation of zebra fish is studied in relation with the infection by M. marinum. The group works on several organometallic drug candidates active versus Plasmodium falciparum, Trypanosoma brucei sp., Mycobacterium tuberculosis. These compounds are the results of finely designed synthesis and the relevance of this topic relies on the threat on human health recognized for these pathogens. Crystallographic studies are at the basis of developing mannose-derivatives as anti-adhesive compounds against uropathogenic E. coli.

Assessment of scientific quality and outputs

The scientific activity of this team is excellent with high level of interdisciplinarity, with members displaying complementary skills, from organic synthesis to cell biology. The research topics cover many different aspects of actual relevance: they span from structural analysis of macromolecules (glycoconjugates or proteins) from recognized bacterial pathogens (mycobacterium, candida etc.) to drug design. In each domain, the team has been able to develop an integrated approach based on highly technical analysis of glycosylation. The attitude of the team is to explore all the potentialities of each avenue opened and the results achieved are excellent.

Since 2008, the team has published more than 120 papers in international journals including 52 as main investigator (first or last author), several book chapters and filed 4 patents; importantly, the number of publications has considerably increased over the last period, from 12 in 2008 to 32 in 2012. Most publications appear in journals of the first quartile, but the Team has produced also 21 papers with IF higher than 5 (good ranked journals) and one publication in Chem. Rev. (IF 40), an extremely prestigious journal.

Assessment of the unit's academic reputation and appeal

The team has an outstanding activity in science dissemination, giving more than 80 contributions, prevalently at international congresses, with 20 of them upon invitation. In this frame, the team has co-organized international workshops (French-Japanese and French-Ukrainian) and seminars in France. The team has attracted four foreign visitors: one Japanese post-doc, and three researchers with international recognition.

The team had the support of 19 grants, both national (two ANRs as coordinator, and three as participant) and international, and the team is coordinator of 12 of them. This includes international exchange programs such as Procope (Germany), Elletra (Italy) and JST Japanese French cooperative program. The team is involved in other five scientific networks including a Bio-Asia consortium. The group co-manages the NMR platform at the Lille 1 university, and manages the liquid chromatography and gas chromatography services both at the UMR CNRS 8576. The group developed an on-line database of carbohydrate structures, Glycobase, with glycosides from zebrafish. They created and managed the platform PAGés, dedicated to glycan and glycoconjugates analysis from any origin.

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

The team has made considerable efforts to increase the transfer of basic research toward the industry through patenting and licensing. The team made four patents: two deal with the development of new synthetic drugs (one in collaboration with Sanofi); the other two relate with the work on Candida (supported by Biomérieux and SATT Nord de France) and the work on the abscidian Halocynthia roretzi. Pre-industrial projects are under maturation with SATT Nord de France (one project accepted and one project under reviewing) and the industrial sector. The team also participates in CNRS National Committee and Specialist Committees CNU 64-65.

Assessment of the unit's involvement in training through research

The team manages Licence level 'Biologie parcours Biochimie', training periods for 'Ecole Polytechnique de Lille'; Masters in 'Chimie et Biologie', 'Biologie et Biotechnologies', 'Génomique et Protéomique', 'Nutrition, Sciences des Aliments et Agro-alimentaire'. The team has trained three PhD students, and two others are still in progress. These students have all contributed to the scientific production of the group and several prices (thesis, posters..) have rewarded their work. The team is also involved in a student exchange program (2012- UGent-Lille cooperation and NASU-CNRS Cooperation) and in the Japanese-French Cooperative Program.

Assessment of the strategy and the five-year plan

The future activities proposed by the team are excellent in meeting the emerging concepts in glycochemistry and glycobiology, such as e.g. glycan imaging. The team will continue on the issues left opened from its present research topics and will develop new issues. The project on catabolism enzymes from mycobacteria will focus on D-arabinases, their biological functions and biological activity of their products. The team will work also on the synthesis of substrates and inhibitors of these enzymes. The group will analyze the effect of E. coli fimbriae adhesion on the glycosylation of superficial epithelial cells and on the preparation of new compounds through innovative synthetic approaches in collaboration with Nantes. The team will study also a set of ricin-like lectins from Mycobacterium, for which the ligand is still unknown. The team will develop monosaccharide analogues for imaging using Raman microscopy, and organometallic-azido molecules for microscope visualization via TEM. Indeed, the future plans are sound and consistent with the team capabilities, whose configuration and managing ability guarantees a wise problem examination, the capacity of adaptation/solution to emerging complications, and the change in strategic direction in response to emerging needs.

Conclusion

- ***Strengths and opportunities:***

This team has a high level of expertise in glycobiology, international and national visibility, and a high research potential sustained by appropriate recruitments. The various approaches and models developed are strong basis for future research. The interdisciplinary environment, with recent inclusion of synthetic chemistry and crystallography, should appear very attractive for students. The strong interest from pharmaceutical companies will develop, with the help of the analysis platform.

- ***Weaknesses and threats:***

The team expertise is dependent on sophisticated technologies and access to most recent apparatus is not fully secured. The analysis platform success also depends on financial input for the maintenance of the spectrometers. The team will be the larger one in the next period and special care should be given in order to secure and stabilize all young researchers.

- ***Recommendations:***

The committee recommends to distinguish clearly the platform activity from the specific research activity pertaining to the team and possibly to make it more visible (participation in national network and certification such as ISO9001). The visibility of both the team and the platform could be enhanced by better managing of a web site. Taking into account the expertise of the team and the quality of the results, a more ambitious strategy for publication and for application to prestigious international grants could be setup.

Team 2: NMR and molecular interactions

Name of team leader: Mr Guy LIPPENS and Ms Isabelle LANDRIEU

Workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent researchers from Institutions and similar positions	3	3
N3: Other permanent staff (without research duties)		
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	2	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	6	4

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

Detailed assessments

The team "NMR and molecular interactions" uses high field NMR to understand the relation between structure and function of different proteins by studying their conformation, their interactions and their chemical modifications. The team has obtained significant results by developing biomolecular structural studies in a close relationship with biology on important health problems: Alzheimer disease, inflammation response and Hepatitis C virus pathogenesis. In particular, the team has been pioneering in the understanding of the relation between phosphorylation and some cellular dysfunctions induced by Tau pathogenesis. Along with phosphorylation, the team has investigated another post translational Tau modification, the O-GlcNAcylation, which in vivo contrasts the effects connected to hyperphosphorylation. In parallel, the group is developing a collaboration with Team n°7 on inflammation response with focus on Cyclophyline ß-mediated regulation pathways. Another collaboration (IBCP, Lyon) focused on a viral protein essential in the hepatitis C virus (HCV).

Assessment of scientific quality and outputs

The team has demonstrated its strong capacity to correlate biological data with structural and dynamic molecular behavior. They have explored biomolecular NMR at its full potentialities to answer to some important biological questions and they have developed an outstanding research. The characterization of post translational Tau modifications represents an important contribution to the field of neuronal associated disorder proteins. The results obtained on essential and difficult viral proteins involved in the HCV replication represent a real breakthrough in the HCV field to understand the role of these enzymes at the molecular and cellular level.

The team has produced 52 publications in international peer reviewed journals including 22 as main investigator, two book chapters, and deposited 6 records of protein NMR assignments in the BMRB database. Moreover, the team has published 9 papers in extremely qualified journals such as Angew. Chem., Nucleic Ac. Res. and Faseb J.

Assessment of the unit's academic reputation and appeal

The team performed excellent scientific dissemination through poster, oral and invited communications in different national and international conferences. From a total of 50 contributions, 14 were upon invitation and cover in a homogeneous manner the different scientific issues developed by the team. The team is involved in both national and international collaborations groups with Dortmund and Berlin on the molecular and functional characterization of the phosphorylated Tau2, and Heidelberg and Lyon on viral replication of HCV virus. All these collaborations are well established and highly productive as demonstrated by the number of publications.

In the last five years, research of the team was supported by 9 national competitive grants (ANR, ANRS…) some as coordinators. The team is part of an EU program for industry-academy partnerships (IAPP) and is also involved in two scientific networks: Fédération TGIR RMN Très Hauts Champs - FR3050 CNRS and the regional NMR group. They actively participated to the biomolecular visibility of the National NMR platform shared between biomolecular and material sciences. The team organized the Scientific Committee TGIR and User meeting (2012).

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

The team interaction with the social - cultural environment is based on its NMR expertise and is outstanding. The team contributes to the local LABEX Distalz project (Development of Innovative strategies for a transdisciplinary approach) with the aim to develop new biomarkers and new therapeutic targets of the disease. The team has the proper and complimentary partnerships with academic and industrial partners on the basis of solid scientific and economic interests shared from the two sides: the team has 5 contracts with national (Servier) and European companies (Complix, Debiofarm, Intervet). During a research contract with Debiopharm, they have contributed to the development of Debio 025. This non-immunosuppressive compound displays in vivo anti-HCV and anti-HIV (Human immunodeficiency Virus) activity.

Assessment of the unit's involvement in training through research

The team has trained 4 PhD students and education of other 4 PhD students is now in progress. The trained students have all contributed to the scientific production of the team in terms of publications. The team has now 5 post-docs under contract and has trained 11 students from Licence to Master level. In this group, students are trained in a multidisciplinary context including different fields such as structural biology, NMR Spectroscopy, molecular biology. The team gives one course in the UE Master in Biological Chemistry entitled "Proteins and biomolecular interactions" and participates to the operation of the NMR platform that is included in the national TGIR "RMN à très haut champ". In this context, they regularly advise and assist different national users in their NMR experiment design. They have also organized a CNRS training course in 2010 on "Non linear sampling in high field NMR spectroscopy".

Assessment of the strategy and the five-year plan

The team has delineated in a clear manner the research plans for the next five years and these are the rational development of the research conducted in the past years. The strategy plan focuses i) on post translational modification of the neuronal Tau protein, and ii) on the HCV RNA replication and the characterization of the cyclophilin (Cyp) prolyl cis/trans isomerases (PPIases). The perspectives proposed by the team appear promising. Due to the medium size of the group, the strategy is based on few strong collaborations. Internal department collaboration will also be reinforced and few different grant applications have been proposed. The future topics have an academic and also industrial interest. As new issues, there are those acquired through the LABEX Distalz platform. Interest in an industrial context is given in the EU project, centered on the search of new compounds modulating the interaction phospho-Tau/14-3-3 complex, these compounds, provided from the industrial partner Lead Discovery Center, could potentially be developed as therapeutic drugs.

Concluding, the activity of the team is appealing for industrial partners and joins basic and applied research; the competence in NMR allows the team to develop or to apply to other topics if the contingencies will require, and its strong NMR expertise increases the probability of successful handling even of risky projects. The team has well delineated its future research in terms of both scientific and technical feasibility, all topics are of social interest and amenable to yield results in the next five years.

Conclusion

- ***Strengths and opportunities:***

Based on both its strong and solid collaborations with excellent groups and its capacity to adapt and develop their technology, this team will certainly continue to contribute significantly to biological questions of high interest. The access to high field NMR makes this team appealing for scientists or young scientists sharing interest on NMR as analytical tool applied to biochemical – functional issues. Their leading role in the project of a 1.2 GHz NMR could further increase the visibility of the team and the attractiveness of the department. This spectrometer could open new opportunities to resolve some of the most challenging biological questions.

- ***Weaknesses and threats:***

The coherence of the team may be weakened by an augmentation of the biological questions addressed. The limited participation to the university teaching process may be a limitation for attracting students.

- ***Recommendation:***

The size of the team is a limiting factor to develop efficiently at the same time their own structural biology subjects and the topics started in collaboration with the other teams of the department.

Team 3: Microbial Genetics

Name of team leader: Mr Steven BALL

Workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent researchers from Institutions and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**4**	**4**

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

Detailed assessments

The team "Microbial Genetics" conducts forefront fundamental research in the area of storage polysaccharide metabolism in microorganisms. The team contributed a number of major scientific achievements: 1) Discovery of starch in the diazotrophic cyanobacteria leading to the proposal that cyanobacteria donated plastids to plants via endosymbiosis and conclusion on convergent evolution; 2) Study of the starch metabolism machinery in a common ancestor of the plant kingdom, Archaeplastida related to the plastid endosymbiosis; 3) Discovery that major carbon translocators are related to the NST3 family of endomembrane transporters; 4) Discovery of SSIII-SSIV glucan synthase in Cyanophora paradoxa inferring that this organism lacks a glycogenin type primer; 5) Discovery of the chlamydial pathogen origin of a glucan synthase gene needed for symbiotic flux in plastid endosymbiosis and secretion of a virulence effector to attach the symbiont to host and pathogen in a tripartite symbiosis. This finding has perhaps connection with metabolic integration of the mitochondrion.

Assessment of scientific quality and outputs

During the last years, the team obtained outstanding results in the domain of starch biosynthesis and mobilisation as it occurs in unicellular algae. The topic holds tremendous value of its own as well as translational value to higher organisms and brings in fascinating facets from evolutional biology particularly significant in expanding insights into the evolution of gene networks relevant for starch metabolism in plants. All together the Microbial Genetics team presents a stronghold in searching for new understanding of fundamental biological processes. The elements of interdisciplinarity of the team's research are particularly prominent concerning fundamental principles in molecular evolution and development of organisms.

The originality, scope and contribution to advances in the field are at the international forefront as reflected in publications in top journals, including Nature, Science (both concern multi-authored papers on genomes), Trends in Plant Science, PNAS, Plant Cell, Plant Physiology, Molecular Biology and Evolution and Nature communications. The team in the period published 26 papers including 16 as main investigator. Many articles were coauthored by leading international groups in the field and also co-publications with experts on starch structure. The team seeks to publish with high impact and has a very high international recognition and reputation.

Assessment of the unit's academic reputation and appeal

The team influenced the international community and provides inspiration to the field with impressive impact. It has participated in 3 national ANR grants, two of which are being coordinated by the team leader, and in other national scientific network collaborations with funding (PEPS, IFMAS). The team has numerous international collaborations including visits of leading international scientists in the field. One of the young researchers received the Bronze Medal from CNRS. The team leader is a delegate in agronomy ecology and environmental sciences at AERES and was in 2012-13 coordinator of the whole research area devoted to this sector. The team made a large number (25) of presentations upon invitation at important international and national meetings. The team made press releases on an antimalarial vaccine and genomic sequence of Chondrus crispus and this was highlighted on the organisations (CNRS, INSB, INEE) websites.

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

The team is mainly involved in fundamental research. Nevertheless, it holds a number of partnerships including a ten year project involving other academic partners within the "great loan" project Institut Français des Matériaux Agro-Sourcés (IFMAS).

Assessment of the unit's involvement in training through research

The team has trained 6 PhD students in the period, including 3 still in the group. They have the scientific level to maintain proficient training of young researchers.

Assessment of the strategy and the five-year plan

A short research plan with five points is described 1) Functional analysis of starch catabolism, 2) The study of glycogen metabolism gene in the chlamydial infection process, 3) Study of cyanobacteria starch mutants, 4) Study of the starch metabolism in Cyanophora paradoxa through the study of mutants, 5) Study of Guillardia theta starch metabolism and mainly the debranching process needed for amylopectin crystallization. The project appears as a continuation of the present research project with a willingness to focus on the functional analysis of enzymes of the starch metabolism mainly through the analysis of mutants and the study of 3D structures of key enzymes.

Starch metabolism is a very debated and competitive domain and the proposed ambitious research involves risks of being unsuccessful. One example is in production of recombinant proteins from cloned genes to gain novel insight on function from their three-dimensional structures. A new collaboration to get such structures has been initiated with the Carlsberg Laboratory. This is obviously risky but has the potential to ascertain hypothesized functions in the starch metabolism of genes which have been identified by a bioinformatics analysis.

Conclusion

- ***Strengths and opportunities:***

The team possesses the drive and capacity to engage in the best partnerships (academic as well as nonacademic) and to achieve goals that are also of societal importance. They developed a very original strategy with a stronghold in a molecular evolution centric approach that is promising for making very important discoveries. The team is able to engage in collaborations addressing applications in the field of biomaterials within IFMAS, particularly on the development of a novel expression system for targeting protein to starch granules.

- ***Weaknesses and threats:***

The team exposes no real weakness, but being rather small may lead to an unforeseen situation where it may be threatened by getting below the critical mass, although the planned research is in accordance with its capacity, including the various opportunities for external collaborations.

- ***Recommendations***

It is recommended that the team is slightly expanded, mainly by recruitment of PhD students and keeps having focus also on international collaborations.

Team 4: Plant Glycobiology

Name of team leader: Mr Christophe D'HULST and Mr Fabrice WATTEBLED

Workforce

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

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

• Detailed assessments

The “Plant Glycobiology” team is involved in the field of starch biosynthesis in plants and has been focusing on fundamental identification of pathways and gene products with assigned specific roles in Arabidopsis by applying a functional genomics approach. The research aims at unraveling the genes and enzymes responsible for specific reactions in biosynthesis in particular of amylopectin, the branched alpha-glucan polysaccharide component of starch. Starch biosynthesis and mobilization are intimately connected also when it comes to enzyme catalysts and a major question addressed has been the trimming of amylopectin during starch granule biosynthesis. This included identification of the functional roles of a number of isoamylase gene products that occur as heterooligomers and have been characterized also in leaves from corn.

Assessment of scientific quality and outputs

The team belongs to the international leaders in the field of starch biosynthesis in plants. They contributed important findings and recently a major breakthrough provided insight into the priming (initiation) of starch biosynthesis in plants. The group conducts research of high quality with great skills and scope that makes contributions to the field of starch biosynthesis at the international level. The group also pursues work on topics of elegant biotechnology where enzymes are used to create novel biopolymers with useful characteristics.

Their publications are in excellent journals for the field with 11 publications during the period with average impact factor close to 6, including 5 as main investigator. The team published research articles in high impact factor journals such as Plant Cell and Plant. Physiol. and a review article in Trends in Plant Science. There is a fruitful collaboration with Team n°3 as seen from his coauthoring of several papers. There are also a few publications coauthored with international leaders in the field and co-publications with national experts in starch structure and enzymology.

Assessment of the unit's academic reputation and appeal

The team has been involved into 3 national ANR programs and one local project. The ISD-starch project has been focusing on the starch metabolism in plants. The Glycoballs project aims at delivering a tool box of amylose elongating, branching and debranching enzymes. Finally, the on-going CaSta DivA (Chloroplast And STarch DIVision Analysis) project concerns the study of the relationship between starch synthesis and plastid division. The team has given 4 oral presentations upon invitation in international scientific meetings on starch metabolism. One international exchange program with Spain resulted in invitation of a student from Sevilla. Two members of the team participated in committees at the ministry and CNRS level.

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

The team is active in biomaterials engineering through a cross-disciplinary national collaboration. They are involved in the “Institut Français des Matériaux Agro-Sourcés” (IFMAS) which is a national project starting in 2013 in the frame of ‘Plan d’Investissement d’Avenir‘. In this context, the team is involved in an ambitious screening project of wheat recombinant inbred lines and potato lines for their ability to synthesize starch granules having characteristics (size of starch granules and amylose contents) that are suitable for bioplastic production. The plant breeding company Florimond-Deprez has appointed a technician for three years to help the team in conducting these screenings.

Assessment of the unit's involvement in training through research

The team has trained 2 PhD students completed in 2009 and 2010 and 2 are currently working on their thesis project. The team leader is responsible for the organization of the course of formal and molecular genetics in first year of Life Science.

Assessment of the strategy and the five-year plan

The scientific project is organized into four axes: 1) CaSta DivA: Identification of the molecular crosstalk. This proposed research project builds on the starch synthase 4 (SS4) being concluded to operate like mammals or fungal glycogenins or being required for formation of a center of nucleation around which the growth of the starch granule is initiated. 2) The implication of branching enzymes in the control of amylopectin crystalline structure will address the interplay between branching and debranching enzymes in starch biosynthesis. 3) Structure – function analysis of enzymes of the starch pathway. On that aspect, the recently recruited assistant-professor will help in characterizing biochemical properties of selected enzymes starting by SS4 followed by branching enzymes and debranching enzymes. 4) Research projects included in the IFMAS involve formation of agro-plastics by engineering starch. This will include large screening of wheat and potato lines for characteristics of interest as well as a targeted approach to study selected granule bound proteins.

Overall the proposed research plans contain several elements of risks, but are at the same time relevant and very ambitious and planned to take advantage of the past achievements and findings. Among these, the study of starch metabolism during the plastid division appears as a very exciting and emerging research project.

Conclusion

- ***Strengths and opportunities:***

The Plant Glycobiology team has a strong combination of scientific skills enabling excellent research including strong national and international collaborations. They are in a very good position to deal with the questions described on the mechanism of various steps in starch biosynthesis and are keen to pursue studies on the structure and function of involved enzymes. The recent recruitment of an assistant-professor offers an excellent opportunity to unravel some molecular and regulatory enigmas in the formation of the starch granule. The IFMAS program is a great opportunity for the team to develop strong relationships with companies in the starch domain and to associate a fundamental high-grade research conducted by the team in the Arabidopis model to applied researches on economically important agronomic plants.

- ***Weaknesses and threats:***

A potential weakness is related to the fact that the current team leader will also be head of the entire UGSF unit and will have reduced time for work on his own research projects. However, several of the projects seem to be well underway and major findings can be expected from the described research plan. The proposed co-leader of the team has a solid profile and this should contribute in maintaining the high-level research carried out by this team.

- ***Recommendations:***

The committee recommends that the team keeps having focus on international collaborations. Also the team should think about organizing training courses (may be in collaboration with Team n°3) in order to increase their national and international visibility and the diffusion of their high-level knowledge.

Team 5: Bacterial envelop genetics

Name of team leader: Mr Jean-Marie LACROIX

Workforce

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

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1.5	
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

The research activity of the team “Bacterial envelop genetics” is focused on the study of osmoregulated periplasmic glucans (OPGs) in bacteria that are glucose-containing oligosaccharides belonging to virulence factors. In particular, this team uses a model organism, the phytopathogen Dickeya dadantii, for studying the biosynthesis mechanisms and the role of OPGs in bacterial virulence. They also developed an interesting approach with the use of the less aggressive Yersinia pseudotuberculosis for the study of the evolution of Yersinia pestis. The team started recently a new project on inhibitors of Pseudomonas aeruginosa adhesion to host cells. The size of the team has been divided by two in the last four years.

Assessment of scientific quality and outputs

Although the scientific community involved in this research area is rather small (with only around 40 research articles published worldwide on this topic over the past 25 years), OPG biosynthesis may be regarded as essential for the entire process of virulence development of Gram-negative bacteria. The team has made an important contribution to this field, with the demonstration that OPGs are directly involved in the regulation of a virulence-relevant two-component phosphorelay RcsCD/RcsB. The team has promising data that should help to understand how OPGs and the RcsCD/RcsB phosphorelay contributed to the evolution of Y. pestis from less aggressive Y. pseudotuberculosis.

The publication score is modest: 12 publications over the past five years, including 4 as main investigator, with a mean IF of 3.9 that however is above the median IF for this domain of research (to be compared with Microbiology, IF 2.4). To be noted, is one publication in PLoS Pathog. (in collaboration) and one in Env. Microb. (as main authors).

Assessment of the unit's academic reputation and appeal

The reputation of the team is mostly national and, consequently, the attraction for young international researchers is limited. The number of communications in congresses is very low: only one oral communication in a national congress is to be mentioned. The expertise in microbiology is recognized by the team being associated to several ANR or charity fundings, therefore securing the finances for the next few years. The team participated in the organization on one national meeting.

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

The activity of the team is mainly focused on fundamental research.

Assessment of the unit's involvement in training through research

The team leader is responsible for coordinating modules in two Master programs. The group supervised 3 PhD students including two who are still in the laboratory.

Assessment of the strategy and the five-year plan

Team members aim to establish a basis on which targets for therapeutic intervention against bacteria can be identified and tested. In this view, the research plan is coherent and open to an interdisciplinary approach, through collaborations with chemists and computational researchers, to search for inhibitors of enzymes involved in OPG biosynthesis. This approach will strengthen the translational aspects of the project and, if successful, should attract industrial partners. The new interest towards Pseudomonas aeruginosa may open interaction with larger community but the rationale for focusing on inhibitors of pili and adhesins is not clear while the team has much more expertise in OPG biosynthesis.

Conclusion

- ***Strengths and opportunities:***

The team has a rare expertise in the study of the biosynthesis and importance of the OPG system in bacteria. They demonstrated expertise in microbiology and the perspectives of development of alternative strategies in antibacterial therapies are important features that should be preserved. The inclusion of "omic" approaches relying on the existing know-how in the academic environment is a very positive development. Funding was sufficient until now (participation in ANR and AFM funded projects, as well as PHRC) and will last up to 2016.

- ***Weaknesses and threats:***

With particular mention to its highly focused research area and limited task force, the way leading to an international visibility seems difficult for this team. A sub-critical size of the team (one technician will leave in 2015) might be a strong limitation in the next future. A substantial part of funding was obtained for a research activity that is not the real core of expertise of the team (P. aeruginosa), with a switch to the search for inhibitors for pili and flagella proteins. There is no striking evidence that the team has the experience required to pursue this project that creates a thematic dispersion.

- ***Recommendations:***

The pertinence of maintaining an independent team of this size is highly questionable. Instead of being independent, this team may profit from being part of a team with high international reputation to gain easier access to (i) modern research technologies, (ii) human and financial resources, and (iii) publication media with higher impact and dissemination. In particular, a closer interaction with research teams that study osmo-regulation in bacteria and possibly P. aeruginosa is needed to gain visibility in the field. The team should also further develop interactions inside and outside UGSF, with particular attention to industrial contracts, and increasing the impact of microbiology within UGSF should be one of its objectives.

Team 6: Regulation of terminal glycosylation

Name of team leader: Ms Anne HARDUIN-LEPERS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	5
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)	2	
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	7	6

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

• Detailed assessments

In the last period, the team "Regulation of terminal glycosylation" set a strong focus at detecting and analyzing the regulation of glycotopes with variant expression in healthy and tumor tissues. The research in the group follows two major lines: (i) Identification of variations in the terminal glycosylation patterns during oncodevelopment (focus on breast cancer) and establishment of relevant analytical (diagnostic) tools to identify these changes; (ii) Molecular phylogeny and functional genomics and establishment of zebrafish as model systems to modulate/reconstruct glycosylation pathways. The team is proposing a change in the team leader position for the next period and will gain two researchers from another group.

Assessment of scientific quality and outputs

The work carried out has delivered major novel insights into the regulation of glycosyltransferases, an information of major value towards the development of therapeutic approaches. An important number of test systems with significant potential for routine clinical application has been established. While correlation between glycosylation changes and cancer is widely accepted, the team is among the few ones that could characterize the involvement of dedicated glycosyltransferases and their regulation, resulting in publications in excellent journals (Cancer Res., Chemistry..) The novel axis on phylogeny of sialyltransferases already lead to impressive data on the reconstruction of the evolutionary history of Golgi-associated glycosylation.

The team has an impressive publication record, with 33 publications, including 22 as main investigator, in highly ranked journals in the domain of glycosciences (JBC, Glycobiology) or cancer sciences (Mol. Cancer Res., Breast Cancer Res., Cancer Res.). The have numerous international collaborations, significant extramural funding, and a number of invited talks in international conferences. The team also contributed to the development of a database on Glycosyltransferases (GT-database).

Assessment of the unit's academic reputation and appeal

The research of the group is based on national and international collaborations (UK, Korea and Portugal), including clinical researchers. They have been successful in competitive national funding calls, with coordination of one ANR project and of several grants from caritative funds.

The team has created a productive international and interdisciplinary network in glycosyltransferases, with far reaching visibility as reflected by many international contributions. The strong visibility of the researchers is attested by the high number of invitations (20) to talk in conferences and seminars. The team leader is the past President of the French Glycosciences Society and organized the last meeting in 2012. The team was also involved in a large number of glycosyltransferase international meetings. The team members participate actively to CNRS national committee and to many expertise committees.

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

The team is mainly involved in fundamental science and has only few contracts with pharmaceutical groups (LFB and Guerbet).

Assessment of the unit's involvement in training through research

During the last period, the researchers were involved in training 10 Master students and in supervising 5 PhDs. The past team leader is co-directing the doctoral school of Health and Life Sciences.

Assessment of the strategy and the five-year plan

This team has given itself a clear and future oriented structure. The two major research lines will be further pursued, but the researchers have also developed intelligent ways to combine their expertise. Future work will contribute to the understanding of how changes in the patterns and functions of glycosyltransferases have influenced species diversification and disease development.

In summary, future research builds on results obtained in the past period and in a creative and solid manner extends toward (i) the production of diagnostic tools and (ii) an improved understanding of evolutionary processes. The two lines will be brought together and will be integrated with analyses that will inform on topological aspects as well as intracellular transport mechanisms that are involved in the fine tuning of the glycosylation outcome. With the joining of two assistant professors from another group (both already recognized researchers), the team will include the question on how glycosylation variation in the gut mucosa correlates with pathogen colonization and development of chronic diseases. The bioinformatic/functional genomic aspect is going to be strengthened and will include the analysis on how glycoconjugates in the gut mucosa influence bacterial colonization.

Conclusion

- ***Strengths and opportunities:***

The team is in the position to build strong projects based on its know-how in the domain of glycosylation and the regulation of glycosyltransferases. The team networks well with other teams of the research unit. The project on gut mucosa analysis with correlation to bacterial colonization is a highly innovative way to disclose factors that determine the disposition for chronic gut diseases and may provide new targets for therapeutic interventions. The integrated bioinformatics/functional genomics approach is ideally suited to shed new light onto the evolutionary forces that determined the expression patterns of glycosyltransferases.

- ***Weaknesses and threats:***

What is chance (see Strengths and opportunities) can also be risk: the future team leader must take care that the different research axes remain tightly interconnected. The phylogeny project is promising but would largely profit from consolidated support in bioinformatics.

- ***Recommendations:***

To fully exploit the competences existing in bioinformatics and phylogenetic analyses, it is recommended to exploit the research unit expertise in bioinformatics by strengthening internal interactions (e.g. Team n°3). The team could set up a more ambitious strategy for publications.

Team 7: Structural diversity of heparan sulphate and regulation of the C response

Name of team leader: Mr Fabrice ALLAIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	4	4
N2: Permanent EPST or EPIC researchers and similar positions	1	
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	5	4

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

• Detailed assessments

The team "Structural diversity of heparan sulphate and regulation of the inflammatory response" was created in 2009, gathering several UGSF members previously working on diverse glycoconjugates in relation with inflammation and cancer. This new team progressively reoriented its activity on a very specific class of highly complex polysaccharides, the glycosaminoglycans (GAGs) - heparan sulfate (HS) in particular, and focused its interest on the regulation of these molecules in the context of inflammation. The group has set up a number of tools for that purpose, including quantitative PCR approaches to follow the expression level of HS biosynthetic enzymes as silencing or overexpressing strategies to modulate HS structure. The team used a variety of cells from the lymphoid and myeloid lineages, and also developed a very interesting model in which macrophages can be polarized toward the M1 or M2 phenotype. In parallel, the group investigated the HS binding activity of a number of proteins, including selectin or the haemagglutinin (HBHA) of Mycobacterium tuberculosis (collaboration with Pasteur Institute in Lille), where they showed that HBHA undergoes structural adaptation upon interaction with heparin.

Assessment of scientific quality and outputs

While the team was well recognized for its work on cyclophilin B and its regulatory role in inflammation, they chose to start new research projects in a competitive area. In particular they integrated new approaches (for example modeling based approaches, which gave rise to a recent paper using molecular docking to describe the heparin-binding domain of fibronectin - Glycoconj J. 2013). With the use of the original models that they developed, the team could demonstrate that the expression level of various HS sulfotransferases depends on the cell lineage and state of activation/differentiation, making their experimental set up very relevant, as many cytokines are regulated by HS.

With regard to the scientific production, the team published 21 papers in the 2008-2013 period, including 7 as main investigator with an average IF of about 4. Amongst them, one can note NAR and J. Immunol., while the reorientation to HS studies has been published in JBC and PloS One.

Assessment of the unit's academic reputation and appeal

The team is partner of a national ANR grant and of a multi-center research project FEDER/région Nord Pas-de-Calais. Team members have been reviewers for ANR, Paris-13 university, Finovi foundation and US National Science Foundation grants and also participated to the scientific committee of the European Cytokine Society (2012-2014). They are members of the National Committee of the CNRS and participated to selection committees of Lille 1 university (section 64-65).

The team gave 20 oral communications, five upon invitation during workshops or conferences. Oral communications in international conferences, as well as international collaborations are however limited, therefore the reputation wideness is mostly national, presumably linked to the recent reorientation of the team's thematic.

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

The team developed several interesting partnerships and consultantships with pharmaceutical and agro-food companies, such as the Institut Pierre Fabre, Endotis-Pharma and Roquette-Frères. During the last four years, this gave rise to as much as eight contracts with non-academic partners. In conclusion, the team has been very successful in attracting external funding from the private sector.

Assessment of the unit's involvement in training through research

2 PhD students defended their thesis during the 2009-2013 period and 2 others are currently in the team. 4 Master 2 Students have been also trained and one Erasmus student (from Bacau university in Romania) spent six months in the team. Several members of the team are also strongly involved in teaching/supervising activities and are responsible of two masters from the Lille university, an engineering degree (CNAM) and teaching modules at the university of Lille.

Assessment of the strategy and the five-year plan

For the next five years period, the main objectives of the team are: (i) to further investigate the mechanism that regulates HS biosynthetic enzymes (sulfotransferases and Sulfs in particular) level of expression and (ii) to explore the mechanisms by which are assembled specific HS motifs, displaying binding and activating properties for inflammatory factors. To this end, the team proposes to investigate the consequences of silencing or overexpressing HS enzymes on the ability of cells to respond to a given stimulus, and in parallel to determine the composition/structural features of the corresponding HS species. Finally, the team wishes to explore the use of HS oligosaccharides, produced by chemo-enzymatic strategies as anti-inflammatory compounds, blocking heparin-binding proteins.

In conclusion, this team has developed interesting cellular models and also set up a number of tools (siRNA, enzyme overexpression) that appear well adapted to their project. Overall, this project is of large interest, and the strategy seems appropriately designed. However, a relatively large number of targets are pursued and might be difficult to reach within a five year period.

Conclusion

- ***Strengths and opportunities:***

The team has set up a number of very interesting tools to either follow or modulate the expression level of HS biosynthetic enzymes and also developed several original cellular systems that are highly relevant to investigate HS function in relation with inflammation. The project stands on solid preliminary observations on the dependence of HS on the cell lineage and on the cell activation state. The team starts building collaborations in the field of HS analysis (Evry) and synthetic chemistry (Orsay).

- ***Weaknesses and threats:***

The five year plan, although very interesting, is challenging and appears very large for a middle size team which is also strongly involved in teaching activity. The correlation between expression level of HS biosynthetic enzymes and HS structure is not straightforward to establish and the expected results might be mostly descriptive. As it is described, the project aiming at localizing/co-localizing the HS biosynthetic enzymes does not appear to be sufficiently integrated to the main objectives. Funding of the project is not sufficiently secured.

- ***Recommendations:***

Overall this project is very interesting and the team addresses a clearly challenging theme. Due to its intrinsic difficulty, it is recommended however to focus it on a restricted number of cellular systems/inflammatory proteins/biosynthetic enzymes. To remain competitive in this rapidly growing field, it will be important to acquire more international visibility, to target higher impact factor journals for publishing future results and to develop collaborations at the international level.

Team 8: Molecular mechanisms of N-glycosylation and associated diseases

Name of team leader: Mr François FOULQUIER and Mr Dominique LEGRAND

Workforce: emerging team

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		4
N2: Permanent EPST or EPIC researchers and similar positions		3
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6		7

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	6	

Detailed assessments

The team “Molecular mechanisms of N-glycosylation and associated diseases” will emerge from the splitting of the large team “Glycobiology of cell signalling and glycopathology”. The new group is focusing on discovery of novel Congenital Disorders of Glycosylation (CDGs) and molecular dissection of mechanisms underlying CDGs. The main results of the team in the past five years have been built on a fruitful collaboration with a Clinic in Leuven, which recruited a large collection of patients with CDGI and II patients. This provided the French group with biological samples from patients with identified and non-identifed defects that helped to identify and dissect new deficiencies. More especially in CDGII patients, the team previously identified novel mutations in the molecular COG complex in charge of intracellular trafficking in vesicular Golgi, leading to major alterations of terminal glycosylation.

Assessment of scientific quality and outputs

The team research contributes to the worldwide analysis of the CDG disorders and is well integrated with this clinical field. Significant contribution has been made by the team and eventhough the field has emerged more than 10 years ago, new patients and new defects are regularly coming in to illustrate the key regulatory points of the highly complex glycosylation processes. The team benefits from the technological platform of the unit and the knowledge in glycosylation processes of the other teams.

The team has made a particular important contribution with the identification of the Golgi protein TMEM165 and its putative role in Ca++ and pH homeostasis. This was reported in three 2012-2013 papers in high impact journals (IF>5) 2 (Nat Gen, Am J Hum Genet, PNAS). The team has also continued to make important contributions to the functions of the COG complex and novel CDGs caused by defects herein. The team has produced six reviews and 28 original publications (most in medium impact factor journals, IF 2-5) in the five year reporting period, whereof 13 are principal contributions originating from the unit. The output is considered excellent and above the norm compared to similar size groups in Europe and abroad.

Assessment of the unit's academic reputation and appeal

The team has developed a strong international network of collaborations through its expertise and has now gained international recognition. The team leader received the Bronze metal of CNRS in 2012 and was invited to 11 meetings and seminars including two Gordon Research Conferences. Another member is coordinating the Federation de Recherche and has been elected on the board of the French Society for Biochemistry and Molecular Biology (SFBBM).The team has been successful in obtaining national grants (2 ANR with one as coordinator), and participates in a European contract on rare diseases (E-RARE). Team members participated in the organisation of three scientific meetings.

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

The team is mainly involved in fundamental research and, through collaboration, in clinical research.

Assessment of the unit's involvement in training through research

The reporting period states 4 PhDs completed with supervisors from the team. All PhD students have had good publications, and one moved successfully to a group with high standard (San Diego, USA) and has continued to produce excellent publications. At least one PhD student is in progress.

Assessment of the strategy and the five-year plan

The team's proposal for the next five years builds nicely on established results from the reporting period with a clear focus on their discovery of TMEM165. Three lines of research are proposed, where 1 and 3 focus on TMEM165 and 2 focus on development and implementation of novel strategies for discovery of new genes involved in regulation of N-glycosylation. The team clearly wants to pursue the TMEM165 story and the outlined strategies are plausible and should be fruitful. The two novel discovery strategies (metabolic incorporation of functionalized monosaccharides and live monitoring of transport of fluorescent shiga toxin) are interesting approaches and if successful they should be productive and valuable for the community. The team proposes to combine these strategies with siRNA targeting of relevant genes for screening of novel genes affecting N-glycosylation and transport. These are ambitious but achievable goals, although the team does not appear to move to the many other related competitive and highly innovative approaches being applied (and reported) in the literature currently such as use of GFP-reporter protein, population screening of N-glycosylation, WES/WGS, haploid cell systems, CRISPR/CAS9 genome editing, etc. The plan is fully consistent with the expertise of the team and the recent findings.

Conclusion

- ***Strengths and opportunities:***

The major strength of the team is its pioneering work on TMEM165 and the positioning of the team as a center for molecular dissection of CDGs in international collaborations. The team is well positioned in the CDG community and their novel discovery strategies may be valuable assays that could further attract international collaborations and funding. The team has good scientific expertise with highly experienced leaders, who are well connected to the clinical aspects with a direct impact on health in rare diseases.

- ***Weaknesses and threats:***

The research subject is a competitive area with limited access to new patients/CDGs. This highly specific niche of research/patients may be difficult to support without international networks.

- ***Recommendations:***

The team should focus and strengthen its cell biology platform for discovery of CDGs and build and expand on its international network to further position it and the unit as a resource center. The team should secure european and other international funding to develop the program and get enhanced visibility. They should engage in national and international training activities in their field and help develop broader training activities for the unit as a whole.

Team 9: O-GlcNAcylation, cell signaling and cell cycle

Name of team leader: Mr Tony LEFEBVRE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	4	4
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	5	5

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	4	4

• Detailed assessments

The team "O-GlcNAcylation, cell signaling and cell cycle" will emerge from the splitting of the large team "Glycobiology of cell signalling and glycopathology". The members of this new group are focusing on the functions of O-GlcNAcylation in regulation of cell signaling and the cell cycle. The team demonstrated that in addition to phosphorylation, O-GlcNAcylation interferes with the activation of the PI3K/Akt and MAPK pathways. Since O-GlcNAcylation is dependent on cell nutrient status, they also explored the relationship with insulin and insulin receptors and are developing a new study on the regulation of fatty acid synthase (FAS). They are also interested in the role of O-GlcNAc in human pathologies by studying the role of O-GlcNAcylation on the regulation of ß-catenin in the context of colorectal cancer.

Assessment of scientific quality and outputs

Over the past five year period the team has become an internationally well recognized player in the field of O-GlcNAcylation. The team has substantially contributed to the role of O-GlcNAcylation in regulation of cell signaling and the cell cycle. The team that consists of five researchers, has produced 31 original contributions, including 20 as main investigator, four reviews, and one commentary in a high impact Nature journal. The publication output of the group is excellent, most publications are in medium impact journals (IF 2-5) but several are published in highly ranked journals such as Diabetes, Mol. Cell Proteom. and FASEB J. Most papers originate from the team and there are few international collaborative contributions. An interesting finding regarding the modification of FAS (fatty acid synthase) cited as in preparation has apparently not yet been published. In this very competitive area, the output is considered of high quality as compared to similar size groups in Europe and abroad. The team has been successful in securing funding at competitive calls from national agencies such as ANR and charity association (ARC and La Ligue). They also obtained funds from regional calls.

Assessment of the unit's academic reputation and appeal

The team established several international collaborations and has been able to attract international coworkers. A bilateral collaboration with Mexico has also been established with support from ECOS exchange program. The team has been successful in attracting external funding, primarily from competitive calls at ANR and charity funds. It is mentioned that there is a planned project within the FP7 framework for 2014 together with groups in Scotland and Belgium. The excellent international reputation of the team as an important player in the field of O-GlcNAc biology is also reflected by the invitations of team members to speak at international meetings and universities (25 invitations on the period). The team leader has also been invited to write a commentary in a Nature journal. The team participated in the organization of one national and one international scientific meeting.

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

Although the team is mostly oriented to basic research, they have been able to develop several collaborations with pharmaceutical industries interested in the potential application of O-GlcNAcylation for diagnosis (Sanofi-Aventis, Promega) or for development of antibodies (Glycoscientific LLC, USA). They have several industrial contracts with companies in Taiwan and China.

Assessment of the unit's involvement in training through research

The team has completed the training of 4 PhD students with good level of publications associated with the thesis work. 2 more PhD students are still in the team. The team leader coordinates the Biotechnology Teaching Master and one member is in charge of modules in another Master. The team also participates in the council of the Doctoral School.

Assessment of the strategy and the five-year plan

The team proposes an excellent strategy focusing on specific pathways in order to elucidate the concept of O-GlcNAc function. This approach generates a lot of visibility, not only in the field of glycobiology but also in the areas where these signaling pathways are of central importance. The team proposes four distinct lines of studies, where the first three have basis at least partly in the team own past substantial contributions. Dissection of the role of O-GlcNAcylation in PI3K and MAPK signaling pathways is clear and a number of good strategies are proposed. Two of these, identification of O-GlcNAc glycosylation sites and OGT inhibitors are to be performed through collaborations but the strategy for the latter is still unclear. Studies of the function of O-GlcNAcylation in the cell cycle are clearly described and should be feasible. The proposed Wnt/¤-catenin studies are straightforward but rely on novel inhibitors. Studies of the OGT/OGA promoters appear to be based on preliminary results that have identified targets to be functionally validated. The proposal follows a natural development in the expertise of the team and includes new avenues.

Conclusion

- ***Strengths and opportunities:***

The team is in position of becoming the leading group in Europe with respect to O-GlcNAc function in cellular signaling. In particular, the role of O-GlcNAc in cell cycle regulation is a very interesting field that deserves further analysis. The developing collaborations with British and Canadian groups can become an important factor for the success of this team. The team leader is highly motivated and already demonstrated his willingness and ability to establish collaborations within the research unit and internationally.

- ***Weaknesses and threats:***

O-GlcNAcylation is a very competitive domain, and without a strong effort on the development of sophisticated analytical methods there might be a risk that the group will not be able to compete at the international level. The team applies good analytical tools (such as modification-specific antibodies), however novel MS-based methods are not developed and not generally used as standard analytical tools.

- ***Recommendations:***

The international collaborations with British and Canadian groups must be formalized by participation in competitive internationally granted projects in order to gain exposure, and to attract international funding. Internal collaboration should also be continued and encouraged, particularly with Team n°11 with exciting new opportunity of O-GlcNAc modification on secreted proteins.

Team 10: Glycobiology of stress related diseases

Name of team leader: Ms Stefania MACCARI

Workforce

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

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

Detailed assessments

The research of the team "Glycobiology of stress related diseases" is in the domain of neuroscience and is focused on the regulation of the hypothalamic-pituitary-adrenal axis that controls stress: this field is part of neuroendocrinology (basic) and psychiatric disorders (medical). The team has a long experience in the regulation of glutamatergic receptors and is well integrated to the field of stress related diseases. This team has developed and validated a rat model (Prenatally Restraint Stressed: PRS) that allows identification of interesting pharmacological targets. The results obtained in PRS rat model by this team, studying this model from behaviour to molecules, are consistent with an epigenetic hypothesis of mechanisms involved in the long-term effects induced by prenatal stress. The hallmark feature of this team is the association between neuroscience and glycobiology with interdisciplinary approaches such as epigenetic or psychopharmacology.

Assessment of scientific quality and outputs

In a field of constant high competition and demand worldwide, the team recently demonstrated a causal link between reduction of glutamate release in the ventral hippocampus and anxiety-like behavior in PRS rats. (J. Neurosc., 2012). Interesting data obtained by this team has also shown that antidepressant treatment corrected abnormalities in anxious/depressive-like behavior and social memory performances in PRS rats. The effect of antidepressant on glutamate release was strongly correlated with the improvement of anxiety-like behavior and social memory, providing an attractive pharmacological target for novel therapeutic strategies (J. Neurosc., 2013). Very interestingly, increasing evidence suggests that glycosylation may contribute to the epigenetic programming of the adult phenotype. More especially, O-N-acetylglucosaminylation (O-GlcNAc), may act as an epigenetic modulator that deserves further investigation, thereby representing a novel molecular switch for gene regulation.

Since 2008, the team has produced 16 peer-reviewed scientific publications, including 14 as main investigator, and 2 books chapters. These include high impact journals (>7) such as J. Neurosci., Brain Res. Rev. and Neuropsychopharmacol.

Assessment of the unit's academic reputation and appeal

This team has an excellent academic reputation and appeal with a high involvement in the international consortium on modern diseases. The team leader was one of the coordinator of the International Scientific Coordination Network, GDRE 691 (2009-2012) "Early programming of modern diseases" (EPMD) that was created in 2009. Due to the success of the bilateral collaboration with a professor at Sapienza university of Rome, the LIA (Laboratoire International Associé) "Prenatal stress and neurodegenerative diseases" was created in January 2013 with co-direction by leaders of both teams. This laboratory is devoted to the study of the relationship between early stress, metabolic alterations and pathological ageing.

The team is mainly funded by charity association (FRM and Fondation de France). The team leader coordinates an ANR project. The team has been able to attract highly recognized scientific visitors and organized several scientific meetings. The team leader has been invited to 13 national and international conferences. 10 posters have been published for the American Society for Neuroscience, 3 of which were selected as hot topics for the American press.

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

The team's leader has a 20 year collaboration with the Department of Neuropsycho-pharmacology of SERVIER (Suresnes, FRANCE). The team leader is involved in scientific committees of the INSERM, CNRS and CNU in Neurosciences. The invited professor was member of the last committee of the ERC European Community.

In the last three years, this team has hosted twice a year a group of high school students for Biology Discovery Days in the universities and has also taken part in joint artistic/scientific events, (Mary's baby - Theatre Diagonale) by providing full access to bench and animal facilities and direct participation of the members of the team. The group has also been involved in scientific/cultural events of the Espace Culture of university Lille1.

Assessment of the unit's involvement in training through research

The team leader is responsible in part of the master "Neurosciences et Physiologie Intégrée" and of the training of L2/L3 and M1/M2 students. The team includes 3 HDR supervisors that allows the direction of PhD students. This team supervises every year students from Bachelor's and Master's degrees of the university of Lille 1 and welcomes Erasmus students, mainly from Italian universities. The team leader was involved in the construction and is responsible of a "DIU SAPA" (Stress addiction and associated pathologies- Lille 1, Lille 2, Lille 3) and participates in the Master of Neurosciences at the university of Strasbourg and to the Euron International Master in Neuroimmunology (www.euronschool.eu).

Assessment of the strategy and the five-year plan

In the five year plan, a particular interest will be given to a post-translational glycosylation that is directly dependent on the neuronal ability to metabolize glucose: O-GlcNAcylation which may in turn modify the protein activity from intracellular signaling pathway until nuclear epigenetic regulation. Work on this post-translational modification will be allowed by the engagement of a collaborative project with Team n° 9 who accumulated a number of evidences on the role of O-GlcNAc in cell cycle regulation as well as in neurodegenerative diseases. This first aspect of the project will fully take advantage of the expertise of UGSF to characterize mechanisms by which PRS programs pathological ageing through impairments of neuronal glucose metabolism. A particular attention will be also given to the involvement of oxytocin and glucocorticoids in the pathological programming triggered by PRS.

A second part of this project will be focused on cellular, genetic and environmental animal models of Alzheimer's disease allowing to dissect how alterations of glucose metabolism in neurons could link ß-amyloids (Aß) to Tau protein hyperphosphorylation.

Conclusion

- ***Strengths and opportunities:***

The team leader has an international reputation with a high capability to integrate her work in international networks. The group set up an animal model of high interest for studying stress related modern diseases. The well prepared collaborative work with 3 teams of the unit makes a valuable taskforce in neuroglycobiology. Collaboration with Team n° 9 on O-GlcNAc regulation in neurodegenerative diseases will help structuring now an integrated approach fully appropriate for the unit. Such a research line is very innovative in neurosciences research.

- ***Weaknesses and threats:***

The small size of the team may be limiting for the future. Increasing permanent human forces will be strongly necessary for the development of the project on the involvement of oxytocin and glucocorticoids in the pathological programming triggered by PRS. The new project focusing on Tau O-GlcNAc and Alzheimer disease brings the team in a field of intense investigation, but more convincing data and some experimental strategies for studying modifications in hippocampus are necessary.

- ***Recommendations:***

According to the taskforce of the team, the third part of the project concerning the participation of olfaction to the integration of stress signaling is probably a second priority.

Team 11: Glycobiology of Olfaction

Name of team leader: Ms Patricia NAGNAN-LE MEILLOUR

Workforce

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

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

• Detailed assessments

The team "Glycobiology of Olfaction" was hosted by UGSF in the last period and is asking for full integration in the research unit. During the visit, the Committee received official communication of the unité sous contrat recognition by INRA and could discuss with the group leader of the opportunities that it may offer to this team.

The team has developed a very novel approach in the field of chemical communication by characterizing the structure activity relationship of animal odorant binding proteins and defining ligand selectivity based on the glycosylation/phosphorylation status of these proteins. Previously, the team also developed a synthetic and efficient pheromone bouquet that has been validated by the breeding industry.

Assessment of scientific quality and outputs

The team recently obtained very promising data on specificity of pig odorant binding proteins towards odorants such as fatty acids or pheromones like testosterone. Furthermore, the team gained the first evidence of O-GlcNAcylation in secreted proteins and proposed that this post-translational modification regulates 10 porcine OBP variants. These very promising data have been obtained in collaboration with other teams of the research unit.

The team is highly interdisciplinary in the sense that techniques are ranging from chemistry, proteomics to behavior and has proven activity in technology transfer to the veterinary field. The team has produced two book chapters and 7 articles, including 5 as main investigator, in journal with medium impact factor including J. Neuroinflammation, BMC Evol. Biol. and Biochim. Biophys. Acta.

Assessment of the unit's academic reputation and appeal

The team leader was expert for "Atelier de Prospectives INEE/CNRS "Ecologie Chimique" and participates to different local committees. The team is involved in several national networks (GDR Ecologie Chimique, GDR AROMAGRI) and an INRA program. Financing is secured by an agriculture ministry grant and collaboration with farming association. The recognition is limited to the national level with three invited talks.

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

The team has strong interactions with "Union Nationale des Coopératives Agricoles d'Elevage et d'Insémination Animale" (UNCEIA), the association of companies in the domain of animal insemination, that finances most of the research activity. The team developed a commercial product –PHEROBULL- which has now reached the market. The transfer of knowledge to the private sector has been very well performed and a patent has been filed in 2010 (Nr F-10 52329), then extended and further licensed to a company in 2013. The invention delivers a breakthrough and interdisciplinary innovation for bovine reproduction with the arrival on the market of a pheromone spray that is the first of its kind.

Assessment of the unit's involvement in training through research

The team obtained the funding of PhD grants through the private sector and has regularly trained PhD and Master students.

Assessment of the strategy and the five-year plan

Over the past ten years, the team has been intensively working for an affiliation with INRA, which has been finally just accepted under the form of an official status designated as "Unité sous contrat". This could reinforce the team's appeal for new researchers.

The scientific team project is of interest, since it is based on the promising evidence for O-GlcNAcylation of secreted proteins. However collaborations have to be extended with other teams of the research unit. Indeed the team activity is very well integrated and complementary to the other teams working on O-GlcNAcylation and would not find a better environment for its study. The priorities of the project will have to be adapted to the size of the team, depending on the arrangement that will be set up between INRA and the governing bodies.

Conclusion

- ***Strengths and opportunities:***

The team research is deeply innovative and may lead to a significant breakthrough very soon. The team leader has been able to integrate the proteomics and glycan structural analysis though facilities offered by the research unit environment. The team demonstrated its ability to rapidly develop a compound into a marketable product.

- ***Weaknesses and threats:***

This very small team did not reach international level yet. The administrative position was not clear in the past with limited support from INRA and the situation is not fully consolidated yet.

- ***Recommendations:***

The committee encourages the team to gain international visibility. The committee recommends that this group maintains a close collaboration with the teams engaged in proteomics and O-GlcNAcylation to further benefit from the well recognized structural expertise of the unit and also to develop interdisciplinary work that can be published in high impact factor journals. The task force should be increased, either by using the new "Unité sous contrat" label for recruiting, or through merging with another team of the UGSF.

Team 12: Plant fibers

Name of team leader: Mr Simon HAWKINS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	7	8
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	1	
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	8	8

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

• Detailed assessments

The “Plant fibers” group is located in another research unit (UMR INRA SADV) of Lille 1 campus and is applying to join UGSF on January 2015. The main research activities of this group concern the impact of lignification on flax fiber quality. Flax is commonly accepted as a convenient model for studying plant fiber for fundamental aspects and also with regard to industrial application since flax fibers are used for textile industry and for the conception of new composite materials (bio-materials). The scientific objective of the team is to understand the regulation mechanisms controlling the lignification of flax fibers in order to modulate their quality. In order to address this biological question, they mainly focused on the development of flax genetic and proteomic resources.

Assessment of scientific quality and outputs

The team has obtained significant results in different areas: sequencing of the flax genome (through participation in international consortium), development of flax microarrays, creation of a flax mutant population for forward and reverse genetics, and identification of the flax cell wall proteome. The screening of the EMS population already allowed the identification of flax mutants with heavily-lignified fibers confirming that hypolignification is under genetic control.

With regard to the scientific production, the team published 20 papers including 13 as main contributor. Average IF is about 4. Noteworthy are 2 papers in journals with higher IF Plant Physiol. (hypolignification in flax stems) and Plant J. (involvement in the flax genome project). In conclusion, the team has gained an internationally recognized expertise in flax fiber biology and has largely participated to the setting up of flax genetic resources that are of great interest for the scientific community working on plant fiber biosynthesis and valorization.

Assessment of the unit's academic reputation and appeal

The team has participated to 3 national ANR grants (Genolin, PT-Flax and NoStressWall), 2 of them being coordinated by members of the team. They have also been involved in one European KBBE program (Fibragen) associating 10 partners, as well as one international consortium (TUFGEN) aiming at sequencing the flax genome. They also actively participated to the animation and the creation of national networks on the plant cell wall biology. In conclusion, the team has demonstrated a strong capability to be involved, as well as to coordinate national and international projects or international scientific consortium. The number of invited conferences (11) is rather low considering the scientific interest of the research conducted by the team.

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

The team is involved in the French “Future Investment” SINFONI project for the promotion of the use of flax fibers in new composite materials. The SINFONI project associates four national competitivity poles and involves 16 private companies and 5 academics partners. In this context, one assistant professor left for a one-year detachment in a company for developing innovative technologies and industrial transfers. People from the team are members of the scientific committees of national technical institutes. Furthermore, they are involved in an applied project including an industrial PhD grant (CIFRE) with a company. The team also organized a national meeting on flax biology for academic and non-academic participants. This team therefore developed many relationships with non-academic partners related to the flax industry in the context of developing emerging technologies related to composite materials dedicated to building and transport industries.

Assessment of the unit's involvement in training through research

Since 2008, the team has trained 2 PhD students and 3 are currently working on their thesis projects. Members of the team are involved in the teaching and organization of a local agro-alimentary master. Furthermore, the creation of a new international master is a major issue since it should be attractive for foreign students that would like to carry out a research activity in plant science. The originality of new dissemination media developed by the team should also be noticed.

Assessment of the strategy and the five-year plan

Once integrated in the UGSF, the team members plan to continue their research on the formation of the hypolignified cell wall. In particular, they will first use their collection of mutants to functionally characterize lignified-fiber and lignin transcription factors. They will also initiate new projects aiming at studying monolignol (the monomers of the lignin polymer) transport, polymerization and deglycosylation, which all potentially represent mechanisms for controlling lignin biosynthesis in plants. This will include the study of enzymes (UGTs, GHs) and ABC transporters. In this context, preliminary discussions have been initiated with the UGSF Team n°1 concerning monolignol glucoside tagging for studying their cell trafficking. A second sub theme aims at understanding how environment factors (stress in particular) and genotype can modify the cell wall structure. Variability of monolignol glycobiology is also considered from an evolution point of view and the team is considering establishing a collaboration with UGSF Teams n°3 and n°6 on that topic. Finally, in addition to the "construction" and "variability" projects, the team will investigate cell wall degradation. In particular they will develop a metagenomics approach to identify microorganisms and characterize genes potentially responsible for cell wall degradation, thereby facilitating fiber extraction. The knowledge generated by this project should provide interesting information allowing a better control of fiber extraction, which could have industrial consequences.

Conclusion

- ***Strengths and opportunities:***

The team has gained an internationally recognized expertise in flax fiber biology and demonstrated a strong capability to be involved as well as to coordinate national and international projects or international scientific consortium. They developed many relationships with non-academic partners related to the flax industry in the context of developing emerging technologies related to the production of new composite materials. This team leaves a plant science lab that will disappear in January 2015. In this context, some permanent people (4 but 2 without any publication in the past contract) will join the team and as a consequence, the team will benefit of additional forces for conducting the scientific project proposed in the document.

- ***Weaknesses and threats:***

Contacts and exchanges of the team with the other groups of the UGSF will not be facilitated until it physically integrates in the same building.

- ***Recommendations:***

Effective integration of this team in the UGSF lab will mainly depend on its capacity to scientifically interact with other teams and benefit on their expertise in glycobiology (tagging through click chemistry strategies, structural analysis, gene evolution, etc). These scientific collaborations would strongly contribute to answer the biological questions that are addressed in the scientific project.

5 • Conduct of the visit

Visit dates:

Start: December 16, 2013 at 9 a.m.

End: December 18, 2013 at 12 a.m.

Institution: UGSF

Address: Avenue Mendeleiev, Bâtiment C9
59655 Villeneuve d'Ascq Cedex
France

Agenda of the site visit

Unité de Glycobiologie Structurale et Fonctionnelle

Director: Mr Christophe D'HULST

AERES scientific advisor: ***Ms*** *Sophie de BENTZMANN*

Visiting committee: *Ms Anne IMBERTY (Chair), Ms Rita GERARDY-SCHAHN, Ms Cristina de CASTRO, Mr Jean-Marie SCHMITTER, Mr Patrice LEROUGE, Mr Henrik CLAUSEN, Mr Marc SAVASTA, Ms Catherine RONIN, Mr Marcus AEBI, Ms Birte SVENSSON, Mr Hugues LORTAT-JACOB (CNRS), Mr Jean-Pierre SIMORRE*

Day one – 16 December 2013

9:00	Welcome (closed-door) Visiting committee with the AERES Scientific advisor
9:15	**AERES representative**: the role and procedures of AERES
9:30	**Direction of the unit:** Past and future, Discussion
10:30	Coffee break
10:45	**Team Biodiversity associated to glycoconjugates**
	Talk and discussion
	Name of the team leader Mr Yann GUERARDEL
11:35	**Team Bacterial Envelope Genetics**
	Talk and discussion
	Name of the team leader Mr Jean-Marie LACROIX
12:25	**discussions with team leaders**
12:35-12:45	closed meeting
12:45	Lunch
13:30	**Team Microbial Genetics**
	Talk and discussion
	Name of the team leader Mr Steven G. BALL
14:20	**Team Plant Glycobiology**
	Talk and discussion
	Name of the team leader Mr Christophe D'HULST
15:10	**Team Plant Fiber**
	Talk and discussion
	Name of the team leader Mr Simon HAWSKINS

16:00	**discussions with team leaders**
16:15-16:30	closed meeting
16:30	*Coffee break*
16:45	**Parallel meetings with personnel:**
	Discussions with engineers, technicians, administrative
	Discussions with staff scientists
	Discussions with students and post-docs
17:15	**Discussion with Doctoral school director**
17h30	**Discussion with the head of the Center**

Day two: 17 December 2013

9:00	**Team Regulation of terminal glycosylation**: Talk (past activities, projects) + discussion including the team leader
	Name of the team leader Ms Anne HARDUIN
9:55	**Team RMN and Molecular interactions**
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leaders Mr Guy LIPPENS and Ms Isabelle LANDRIEU
10:50-11:00	closed meeting
11:00	*coffee break*
11:15	**Team Structural diversity of heparan sulfates and regulation of the inflammatory response**
	Talk (past activities, projects) + discussion including the team leader
	Name of the team leader Mr Fabrice ALLAIN
12:10-12:15	closed meeting
12:15	*lunch*
13:45	**Team Molecular mechanisms of N-glycosylation and associated diseases**
	Talk (past activities, projects) and discussion
	Name of the team leaders Mr François FOULQUIER and Mr Dominique LEGRAND
14:35	**Team O-GlcNAcylation, cell signaling and cell cycle**
	Talk (past activities, projects) and discussion
	Name of the team leader Mr Tony LEFEBVRE
15:25	**discussions with team leaders**
15:35-15:45	closed meeting
15:45	*coffee break*
16:00	**Team Glycobiology of stress related diseases**
	Talk (past activities, projects) and discussion
	Name of the team leader Ms Stefania MACCARI
16:50	**Team Glycobiology of olfaction**
	Talk (past activities, projects) and discussion
	Name of the team leader Ms Patricia NAGNAN-Le MEILLOUR
17:40	**discussions with team leaders**
17:50-18:00	closed meeting
18:00	**Discussion with the representatives of the managing bodies**

Day three: 18 December 2013

8:00-12:00	**Private meeting of the visiting committee (in presence of the AERES scientific advisor)**
12:00	**End of the visit**

6 • Supervising bodies' general comments

Université Lille1
Sciences et Technologies

DIRVED
Direction de la Recherche,
de la Valorisation et
des Etudes Doctorales

Le Président de Lille1,

Sciences et Technologies

A

M. le Président de l'AERES

Objet : réponse au rapport sur l'UGSF
Vos références : E2015-EV-0593559Y-S2PUR150007678-005148-RT
Nos Réf : DIRVED -2014-325

M. Le Président,

Nous tenons à remercier le comité de visite de l'AERES pour le temps consacré à l'évaluation, la qualité des échanges et d'écoute et les recommandations pertinentes proposées. L'UGSF s'engage à mettre en œuvre, dans les meilleurs délais, ces recommandations.

Il n'y a que quelques corrections factuelles mais pas d'observations générales de la part du laboratoire.

Villeneuve d'Ascq, le 10 mars 2014

Le Président de Lille1,
Sciences et Technologies

P. Rollet

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