CIIL - Centre d'infection et d'immunité de Lille

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Centre d'Infection et d'Immunité de Lille

CIIL

Under the supervision of the following institutions and research bodies:

Centre National de la Recherche Scientifique - CNRS

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

Institut Pasteur

Université Lille 2 – Droit et Santé

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,

- Mr Jean-Luc IMLER, 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

Unit name:	Center for Infection and Immunity of Lille
Unit acronym:	CIIL
Label requested:	INSERM, CNRS
Present no.:	UMR 8204 (CNRS) – UMR_S1019 (INSERM)
Name of Director (2013-2014):	Mr Camille LOCHT
Name of Project Leader (2015-2019):	Mr Camille LOCHT

Expert committee members

Chair:	Mr Jean-Luc IMLER, University of Strasbourg
Experts:	Ms Ina ATTREE, Université Joseph Fourier, Grenoble
	Mr Philippe DESPRES, Pasteur Institute, Paris
	Ms Valérie JULIA (INSERM Representative)
	Mr Bernard LA SCOLA, Université of Aix-Marseille (CoNRS Representative)
	Mr François LEULIER, École Normale Supérieure of Lyon
	Ms Olga MATOS, New University of Lisbon, Portugal
	Ms Penelope MAVROMARA, Hellenic Pasteur Institute, Athens, Greece
	Mr Paul MICHELS, University of Edinburgh, UK
	Mr Olivier NEYROLLES, University of Toulouse (CoNRS Representative)
	Mr Pierre PAROT, CEA, Bagnols-sur Cèze
	Mr Jean-Michel SALLENAVE, Pasteur Institute Paris
	Mr Peter VERHASSELT, University of Louvain, Belgium
	Mr Andrew WATERS, University of Glasgow, UK

Scientific delegate representing the AERES:

Ms Sophie de BENTZMANN

Representatives of the unit's supervising institutions and bodies:

Mr Patrick BERCHE, Institut Pasteur de Lille

Mr Régis BORDET, University of Lille 2

Ms Martine LECOUTRE, Université Lille 1

Mr Yves LEMOINE (Representative of Doctoral School n°446)

Mr Bruno LUCAS, CNRS

Mr Samir OULD-ALI, INSERM

1 • Introduction

History and geographical location of the unit

The Center for Infection and Immunity of Lille (CIIL) was created in January 2010. Located within the Pasteur Institute of Lille (IPL), it groups together teams focusing on infectiology, immunology and inflammatory diseases. Indeed, while originally launched at the end of the XIXth century to study, understand and treat infectious diseases, IPL has since then broadened its scope to include other diseases such as cancer, metabolic and cardiovascular diseases, and neurodegenerative pathologies. As a result, teams working on host-pathogen interactions had become distributed in different research units on the campus.

The CIIL was created as a mixed research unit of IPL, INSERM, CNRS, Université Lille 2 and Université Lille 1 with the aim of combining the efforts and resources of teams working before 2010 on infectious diseases and immunology in six different research units from INSERM or CNRS. Initially composed of 11 teams plus a technology platform (Transcriptomics and Applied Genomics), the CIIL was joined by three additional groups since 2010, the emerging teams CGIM (ERC starting grant), and BDEEP and an Atip/Avenir team. Although there is no formal organization in departments, research in CIIL focuses on three major topics : basic and applied parasitology (four teams) ; molecular and cellular microbiology (five teams) and immunity and inflammation (five teams).

All teams of the CIIL are housed on the IPL campus in downtown Lille, but in three separate buildings, which reflects the different origins and histories of the teams. This geographic spreading of the teams, as well as the different status of the personnel (e.g. CNRS, INSERM vs IPL), have been identified as an important challenge for the organization and coordination of the CIIL. In a near future, all teams should be gathered in two separate buildings

Management team

The CIIL is run by an executive Council, which elects a director and a deputy director for a period of five years. The executive council is composed of all team leaders, and meets at least once a month to make decisions on budget allocation, investments (e.g. common equipments), recruitments, organization of seminars and symposia. For the period 2010-2014, the director was Mr Camille LOCHT, and the deputy director was Mr Jean Dubuisson. For the next five year period, Mr Camille LOCHT has been re-elected as director, while the next deputy director will be Mr François TROTTEIN. An external scientific advisory board composed of 8 members provides assistance to the CIIL to reach and maintain high standards of scientific excellence.

AERES nomenclature

SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	21	22
N2: Permanent researchers from Institutions and similar positions	45	47
N3: Other permanent staff (without research duties)	54	54
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	15	14
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	20	22
N6: Other contractual staff (without research duties)	7	5
TOTAL N1 to N6	162	164

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	38	
Theses defended	55	
Postdoctoral students having spent at least 12 months in the unit	27	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	48	49

2 • Assessment of the unit

Overall opinion about the unit

The CIIL was created in January 2010, and resulted from the grouping of research teams coming from 6 different research units. After only three years of existence and for a first term, the overall achievements of the CIIL teams, which had no previous experience at working together, are remarkable and made a very positive impression on the committee.

The scientific activities of the CIIL cover three major areas, parasitology, microbiology and immunity, in which significant progress was made since 2010. Of note, the scientific production attests of a real integration of the expertise of the teams from the CIIL (e.g. roles of TLR3 and Treg cells in malaria pathogenesis ; anti-inflammatory properties of a live attenuated *B. pertussis* vaccine). As a result, the scientific production and the academic reputation of CIIL are excellent.

Continuing a long tradition within Pasteur Institute of Lille, the CIIL has an outstanding interaction with the economic environment, with an impressive number of contracts with industry, patent applications and licensed patents. The CIIL also participated in the creation of a start-up company, and is associated with several clinical studies to translate its fundamental research into novel therapeutic approaches.

The CIIL teams are spread over three different buildings, which, together with the fact that buildings are run by different managing bodies, was perceived as a difficulty. The CIIL has integrated several young teams, and attention should be paid to their consolidation phase, which may be delicate for some of them. For these reasons, communication between the management of the CIIL and the staff is of utmost importance.

Strengths and opportunities related to the context

- CIIL has incorporated microbiologists, parasitologists and immunologists, thus creating a young research unit with real potential for synergy between the different teams, despite the diversity of their fields of investigation;
- seven young groups, with the potential to become well established in the next 5 years, have been created within CIIL;
- CIIL has an outstanding record in translational work and interaction with the economic world;
- CIIL provides a unique environment with cutting edge screening and imaging platforms;
- opportunity to develop ambitious projects on gut microbiota and dysbiosis has been developed with an added value of different teams (LABMI, NLRII, LIII) joining efforts to collaborate and decipher the mechanisms involved;
- opportunity to direct national and international networks (ParaFrap Labex, Paraddise FP7 project) has been seized, which will increase the dimension of CIIL if run properly;
- a new research program dedicated to the emerging MERS coronavirus, which is responsible for severe respiratory disease in humans is proposed: (i) the environment of Lille supports this initiative since there were two hospitalized patients with a fatal case in Lille hospitals; (ii) the program has added value for the development of interactions and synergies with groups working on lung immunity and infectious diseases.

Weaknesses and threats related to the context

- organization and management could be improved (communication, decision making procedures). The panel of PIs seems to be poorly connected with more junior people (PhD students, post-docs) and with the technical staff;
- the current web-site of the institute is not operative in the sense that the current offer does not communicate at any level towards the public or the scientific communauty. Such outreach must be quickly ameliorated;
- strategy on where to put the emphasis for the future: the CIIL has been proactive in bringing new groups, but also appears to want keeping historical groups. The CIIL has to provide space and resources for new groups, which may imply making choices;

- there appears to be a strong demand from research groups for the genomic platform. The platform has been presented as a research group, raising concern that enough resources will be dedicated to this facility. This could be detrimental to both activities.

Recommendations

- diversity of models is a threat and an opportunity. Introduction of a coronavirus research program will add diversity in viral models studied at CIIL, develop interaction between groups working on lung immunity and molecular virology, and also strengthen the links to the clinic. The association between projects on malaria and schistosomiasis appears as marriage of convenience: the only commonality is the drug screening Paraddise FP7 program. It is recommended to provide open access of this facility to other groups, to improve interactions and give chances for cross fertilization. A recommendation is to seek to marry the diversity productively, for example through joint PhDs;
- reinforcement of the virology field has to be supported;
- improvement of the outreach has to be done by remodeling the website;
- an effort has to be made to try to build on shared expertise, through the identification of few programs that could integrate different groups in the next 5 years;
- whether the genomic platform should be kept internal or externalized has to be considered. Resources might be better used to maintain the cutting-edge imaging platform at the top level, rather than running after the pack for sequencing. May be one common platform for genomics, proteomics and imaging, supervised by one manager (Unité Mixte de Service) should be considered;
- access to and utilization of the BSL3 laboratory and animal facility should be made easier to the groups, by reducing whenever possible time consuming procedures and restricting training to the strictly necessary.

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientific quality and outputs of the CIIL are overall excellent. The level of publication is excellent and regular, in the best specialty journals and also in a few general journals (Nature Genetics; Nature Medicine; Cell Host & Microbes; Journal of Clinical Investigation; PNAS). In addition to scientific publications, most teams of CIIL have been successful in raising money from national and international calls, which further attests of the scientific quality and international competitiveness of CIIL. The committee nevertheless noted a tendency to accumulate papers (more than 700 in total for the period 2010-2013), and suggests to push studies further to improve the impact of the publications.

In spite of the overall excellency in terms of scientific quality and outputs, the committee noted heterogeneity between the teams in terms of manpower, project selection and/or leadership, and felt that some of them should be carefully monitored. These include teams led by young researchers (PYP, TAG) and team MSCPGD, which must be encouraged and supported within CIIL to strengthen them. Among these teams, the strategy and projects of the PYP team were found to be promising. Regarding the MSCPGD team, the present head will retire during the next term, raising some concern for the leadership of the team. Renewing funding in three or four years will be crucial. Finally, some questions were raised for the TAG team, which covers both the function of a genomics technological platform and a research team. It is suggested to outsource some of the activities of the facility to maintain it up to the standards, possibly through increased interaction with Gènes Diffusion, and to nurture the research activity within one of the already existing teams. Apart from these young groups, the teams BDEEP and BCIP should also be monitored. The impact of the projects developed by the team BDEEP could be improved by focusing on a single model, which would allow to develop molecular tools and get to cell biology. The BCIP team is addressing very broad questions, especially in light of its limited size. The team has made some nice observations on the contribution of Treg cells in the pathological response leading to cerebral malaria, a promising topic on which the team could focus.

The beneficial effects of joining efforts within CIIL are not yet fully apparent in terms of joint publications, although more than 50 published articles during the period (out of more than 700 in total) result from collaborations between CIIL teams. Of note, these include articles in leading international journals such as Nature Genetics, Journal of Clinical Investigation and PNAS, which attests of the potential of CIIL and of the added value of internal collaborations. The strong potential for synergy between teams of CIIL is also apparent through successful joint grant applications to major national and international calls (e.g. an Equipex ImagIngEx BioMed coordinated by the team CMPI; an European EraNet grant involving the teams MCVH and CGIM; an INCa grant involving the teams LIII and the new team of L. Poulin). Strong potential and interest for interactions between the teams were also apparent during the talks and discussions, with group leaders frequently referring to the work of other CIIL teams.

Assessment of the unit's academic reputation and appeal

The academic reputation and appeal of CIIL is excellent in the field of host-pathogen interactions. The reputation and appeal is attested by the high number of PhD students and post-doctoral fellows trained at CIIL, many of whom come from foreign countries belonging to all continents. In addition, collaborations have been established between scientists from the center and groups in more than 50 countries, placing CIIL in a worldwide network of interactions. The excellence of CIIL is further illustrated by invitations to present data at national and international conferences and to provide expertise in national and international panels (e.g. thesis committees, INSERM or CNRS panels, scientific advisory boards in Germany, UK, Belgium, France). Many CIIL scientists are also on the Editorial Board of national and international scientific journals.

Another readout for the academic reputation and appeal of CIIL is the funding obtained at the national and international level in competitive calls for proposal. At the European level, CIIL scientists have participated in several EU projects, and have in particular coordinated four of them, including the new project A-PARADDISE (2014-2017) dedicated to the development of antiparasitic drugs. In addition, the team CGIM was awarded an ERC starting grant. At the national level, the CIIL has been successful at the highly competitive LabEx and EquipEx calls. The team MCBTG coordinates the nationwide LabEx ParaFrap, which groups together French teams working in parasitology, while the team CMPI coordinates the EquipEx ImaginEx-BioMed that involves four CIIL teams. CIIL has also obtained significant funding from the national research agencies ANR, ANRS, INCa and FRM, as well as from the Region Nord-Pas de Calais.

The CIIL is proactive in increasing its reputation and appeal. It has organized several events since 2010, which contributed to increase its visibility. These include seminars by invited outside speakers (about 30/year), but also the organization of workshops and symposia, both at the national and international level (13 for the period 2010-14).

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

The interaction of CIIL with the social, economic and cultural environment is remarkable.

At the social and cultural level, CIIL is very proactive in the dissemination of knowledge to the public. CIIL scientists communicate well with the media and are frequently interviewed by radio and TV networks, as well as by newspapers. They also participate to cycles of conferences for the general public in France and in Belgium, and are strongly involved in the open house days of the Pasteur Institute in Lille. Under the impetus of the CMPI team, the CIIL is also organizing original activities to target school children (« Kid campus » operation) and teenagers (« Les Apprench'ti Chercheurs » operation).

At the economic level, several teams from CIIL interact with major national and multinational companies, including major players in the biomedical field such as Pfizer, MSD, GSK, Sanofi. Nearly 50 research contracts with industry were awarded to CIIL teams since 2010. The output of CIIL in terms of intellectual property is impressive, as 22 patent applications have been filed during the last five years, many of which have been licensed. In addition, the original discovery that Endocan can be used as a marker for sepsis led to the creation of the start-up company LungInnov by one team of the CIIL in 2009. CIIL is also developing very interesting translational research thanks to the MDs present in the Center (encouraged by the CHU Lille, which emphasized the importance of training by research for its staff), but also through strong interactions with clinicians in CHRUs in Lille and other French cities, or abroad (e.g. India, Senegal).

An important concern relates to the insufficient quality of the web site of the institute that must be improved. Clearly, the current web site does not effectively engage at any level with the public or the scientists.

Overall, CIIL has been remarkably successful in coupling excellent academic research at the fundamental scientific level and translational research leading to innovation and valorized intellectual property as well as to improved clinical practice. The recommendation is to continue on these tracks.

Assessment of the unit's organization and life

The CIIL has managed to integrate existing groups with complementary sets of models, expertises, techniques. The Center also managed to attract promising new groups with either ERC or Atip/Avenir funding. There is strong incentive for the teams to collaborate in joint research, but the Executive Committee does not drive the organization of the collaborations. Indeed, the organization of CIIL is decentralized, and lots of freedom is granted to the teams for grant applications, or the recruitment of students and post-doctoral fellows. The fact that the laboratories are spread on the campus, in buildings run by different managing bodies, was perceived as a difficulty. This makes the level of integration/collaboration already achieved within CIIL quite remarkable. Clearly, greater coordination between managing bodies would be helpful to push further the integration of the participating teams.

In spite of successful integration of the teams within the CIIL, there is room for improvement in the future. In this regard, the committee recommends to take special care of communication between the management of CIIL and the staff, as well as among staff. This seems particularly important at a time when worries regarding the future (e.g. allocation of laboratory space, financial situation of IPL) are tangible, in particular in the context of the heterogeneous private *vs* public status of the technical staff. In this regard, the « conseil de laboratoire » should meet on a regular basis, under a defined yearly schedule. The meetings of the « conseil de laboratoire » should be advertised to the whole unit, and a report describing the points discussed and the decisions made should be circulated among the staff.

One detrimental consequence of the spread over different buildings, run by different bodies, is the lack of common rules/structures for biosafety, hygiene and security according to national and european regulations. A common set of rules and procedures should be defined and enforced for all CIIL personnel. The existence of a BSL3 facility, including an insectarium allowing a unique opportunity to study the interaction of Y. pestis with flees, is a strong asset of the CIIL. Yet, constraining safety procedures for its use bars the CIIL personnel from fully benefitting from it, and appears to cause significant loss of time, in particular for PhD students and post-doctoral fellows. The Expert Committee recommends that a BSL3 User Committee be set up to establish a dialog with the safety officer in charge of the facility. This Committee should include the Director and Deputy Director of CIIL, as well as

representatives for Safety and Risk Prevention from INSERM, CNRS and Lille University. One issue that should be dealt with as a priority by this Committee is the possibility for the facility to accommodate experiments with a new viral pathogen (the coronavirus MERS).

Another point of concern for the communication and exchanges between the teams of CIIL is the lack of informatics coordination between the different buildings hosting CIIL. Care should be taken to improve coordination of informatics when reallocation of the teams in two buildings will occur.

Finally, the potential for interaction between students/post-doctoral fellows is enormous, but only partially exploited at this stage. It should be fostered by providing funds to invite speakers on topics related to not only immunology but also virology, parasitology and bacteriology. Diffusion lists for the technical staff and the students/post-doctorants should be set-up to promote communication among the personnel. The joint supervision of students by different PIs should also be encouraged to promote collaborative work and synergy between the teams.

Assessment of the unit's involvement in training through research

The involvement of CIIL in training through research is overall excellent. At the doctoral level, CIIL is affiliated to the Doctoral School « Biologie et Santé » (ED#446) from the universities Lille 1 and Lille 2. This Doctoral School requires at least one publication submitted as first author to defend the PhD, and claims that 95% of its former students are employed, many of them as post-doctoral fellows. 34 PhD thesis were defended in CIIL since 2010. Progress of the work of PhD students is followed by a thesis committee, which comprises the director of the team, one other member of CIIL (internal reviewer) and one external reviewer. 25% of the PhD students from the Doctoral School « Biologie et Santé » work in the field of infection and immunity, and the CIIL has a strong potential to attract new students to the universities of Lille.

At the Master level, many scientists of CIIL actively participate to the training of students in the laboratory, but also in classes. In particular, four courses on Microbiology, Genomics, Parasitology and Host-Pathogen Interactions are directed by members of CIIL. CIIL teams are also responsible of 10 thematic days, organized in the framework of the Master program in Lille. Finally, several members of CIIL have been invited to lecture Master students in other universities in France (Paris, Lyon, Orléans,…) and abroad (Finland, Senegal, Venezuela, Mexico, …).

The teams from CIIL are also involved in international training, through student exchange programs such as Erasmus within Europe, or the Howard Hughes Medical Institute with the USA. In addition, some CIIL scientists participated in three EU Training Programs (ITN, TB-TEA, TB-PALNet), and in international courses (EMBO courses, international summer schools).

Assessment of the strategy and the five-year plan

The strategic plan for the years to come is to continue developing both fundamental research projects in the field of host-pathogen interactions and immune dysfunction, and translational research to bring to the clinic new tools (diagnostics, therapeutics, vaccines) to control the viral, bacterial and parasitic diseases studied by CIIL teams.

The projects proposed by CIIL teams are, for the most part, original and ambitious. Some projects (e.g. BDEEP projects on the protists Blastocystis and Cryptosporidium, TAG projects on non-coding RNAs) lack originality, but the classic parasitology that is proposed by BDEEP has to be done before the team can move on to more exciting topics such as the cell biology of these organisms. Other teams are encouraged to consider broadening the scope of their screens (e.g. MCVHC efforts limited to the entry/assembly steps) or the selection of protein targets (e.g. MCBTG focusing on known proteins) to increase the impact of their work : in view of their previous achievements these teams can afford to be more ambitious. The risk associated with any ambitious research strategy is in general well balanced for CIIL, either by the strong expertise and the availability of reagents and preliminary data (e.g. the nice niche established in lung immunity by the team PI), or by the existence of cutting-edge technological approaches (e.g. atomic force microscopy for the project of the team MPI). The committee however adds a note of caution for the young teams PYP and MSCPGD, albeit for different reasons: the five year plan of PYP is very ambitious but very broad. Even though the PYP team leader has established a powerful and original experimental system, as well as collaboration with several other groups, a risk exists that a lack of focus will be detrimental for the competitiveness of the group. Regarding the plan of team MSCPGD, it heavily relies on chemical screens, a very demanding approach for which it is not clear if the new team leader has previous experience. This risk can however be modulated by interactions with other teams of CIIL.

Regarding the scientific policy and strategy of CIIL as a whole, a strong emphasis should be put on the continued development of interactions between the teams of CIIL and the development of synergies. The successful integration of efforts conducted in the different teams will require improved communication within CIIL. The overall vision and strategy must be shared with all the personnel, including the technical staff and post-doctorants/students.

The strengths of CIIL for the years to come are adequately presented, and include (i) the development of research projects on topics of major concern for the public health, covering both fundamental molecular and cellular biology, host-pathogen interactions and clinical studies; (ii) strong connections with industry; (iii) involvement in field studies in Africa and India; and (iv) access to cutting-edge facilities. The weaknesses of CIIL, as presented in the SWOT analysis, center on the lack of adequate laboratory space and permanent technical and administrative staff. In this regard, it will probably be difficult to welcome new teams to explore new projects (e.g. Coronavirus, Pneumocystis), and strategic choices will have to be made regarding the priorities of the CIIL.

4 • Team-by-team analysis

Team 1: Molecular and Cellular Biology of Toxoplasma Gondii (MCBTG)

Name of team leader: Mr Stanislas TOMAVO

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	**8**	**9**

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

Assessment of scientific quality and outputs

The team follows standard cell biological events of retro and anterograde transport and looks to see how they function in the Apicomplexan specific cellular features i.e. invasion-associated apical organelles. The research, performed on Toxoplasma gondii is well focused. Currently and even more so planned for the future, the team places a strong emphasis on proteomics. Publication outputs have improved considerably: the team has recently published a number of high quality papers (in particular in Cell Host & Microbes, PLoS Pathogens). The team has published 14 papers since 2008. These include 9 as main contributors in Cell Host & Microbe, PloS Pathogens, Mol Cell Proteomics, Mol Cell Proteomics, Mol Microbiol, J Mol Biol and 2 PloS One. Finally, the team has published 2 invited reviews as a main contributor in PloS Pathogens and Int. J. Parasitol.

Assessment of the unit's academic reputation and appeal

The reputation and attractiveness is solid and appears to have improved as a result of the recent wave of publications. The team leader has contributed a number of reviews including recently one relatively high profile review in PLoS Pathogens. This will all improve the group's profile and likely lead to a better quality of PhD students and post-doctorants applying to work in the team. The national profile of the team leader is upwards as indicated by both his Award of Excellence from CNRS and his appointment as Scientific and Executive coordinator of the national LabEx Parafrap. Recruitment attests of the dynamism of the team: one MCU with a Chaire d'Excellence and one researcher (CR), who has since obtained an ANR-JC grant, have joined the MCBTG team. The head and team members have organized kick off meeting of LabEx and symposia in France and abroad, and the head has been invited speaker and chair at the XIII International congress on Parasitology, at the McGill University (Canada), University of Chicago (USA), Imperial College (England), University of Cambridge (England) and University of Dresden (Germany) during this assessment period. The head of the team has participated as editor or invited editor to the journals PloS One, BMC Bioinformatics and invited editor of PloS Pathogens and was Representative Officer of Cell Biology, Virus and Parasites, INSB, CNRS (2009-2013).

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

The team displays various activities in this respect, including interviews for the main press or TV on *Toxoplasma*, general public conferences, and two patents. A lot of core funding is local so the efforts of the team are effective.

Assessment of the unit's organization and life

Organization is effective given the output. The ratio of permanent staff compared to the number of PhD students and postdoctorants is surprisingly high and the number of young scientists is quite low.

Assessment of the unit's involvement in training through research

Staff members are involved in teaching at the university. The team currently trains 2 PhD students and 2 post-doctoral fellows. In addition, 2 PhD students have graduated in the last 5 years. This number is expected to increase given the current size of the permanent staff that have just or will defend their HDR.

Assessment of the strategy and the five-year plan

Plan is to further decipher the molecular mechanisms of protein trafficking and post-secretory vesicle biogenesis in Toxoplasma gondii, using as a lead the sortilin-like molecule TgSORTLR identified by the team. The plan is fine as far as it goes and given the space available, and the prospects for the understanding of directed molecular traffic in apicomplexan parasites, a critical step of their life cycle, are interesting.

The decision to focus on proteins already characterized in other systems (e.g. sortilin, adaptin) limits the risks of the project, but may also impact on the originality of the findings. There are some worries about the inducible system: no alternative plans are given if it is leaky. No list of priorities is given where there are large lists of candidate molecules to be investigated. The impact of discovering DNA control motifs is not clearly explained. Finally, regarding the validation of retrograde proteomes, it is not clear how much noise there will be in the experimental approach chosen, and it would be good to consider alternative approaches.

Conclusion

The team MCBTG is in a good phase after a period of significant weakness. The team leader has assembled a group of competent people around him, and is developing interesting projects on the important parasite Toxoplasma.

- **Strengths and opportunities:**

- upward trajectory, after a difficult period;
- increased size of the team, indicating improved attractiveness to young students;
- great infrastructure for proteomic analysis.

- **Weaknesses and threats:**

- lack of clarity and details in presentation of the research plan, in particular regarding possible alternative strategies (e.g. to address the leakiness of the current inducible system);
- lack of originality by preferentially studying proteins already characterized in other models. The corresponding transport system may have already been defined, thus limiting novelty and impact of the work.

- **Recommendations:**

The team has to improve organization and to define in a more detailed manner its experimental plan. It should also build an attractive website (even if outside of official CIIL site). Now that it has obtained a good national recognition and visibility if the field of parasitology, the team is also encouraged to explore the possibilities for developing more international contacts and activities.

Team 2:

Molecular Signaling and the Control of Parasite Growth and Differentiation (MSCPGD)

Name of team leader:

Mr Jamal KHALIFE

Workforce

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

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended	7	
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	4	4

• Detailed assessments

Assessment of scientific quality and outputs

This team is composed of two subgroups with different interests and expertise, and is the result of a recent fusion. Leadership is changing due to the forthcoming retirement of two professors. One subgroup works on epigenetic mechanisms and kinase-based signaling in the helminth parasite *Schistosoma mansoni*, the other focuses on a specific protein phosphatase and signaling in *Plasmodium falciparum*. Both projects are meant to better understand the biology of the parasites and host-parasite interactions, and to contribute to developing therapies. The team underlines in the report the fruitful exchange between the different research lines, but at the same time expresses its plans for a better integration in the future (on the common theme of 'signaling'). The unifying feature is the PARADDISE project looking for inhibitors of the writers, readers and erasers of the epigenetic code and for which significant funding has been leveraged. The scientific quality of both subgroups is high, and yielded a highly respectable output, both in quality and in quantity: the *S. mansoni* subgroup published more than 40 articles, including some 20 as main contributors, in journals such as PLoS Pathogens (3), PLoS Neglected Tropical Diseases (3), Trends in Parasitology (2), but also Nature (genome of *S. mansoni*); the *P. falciparum* subgroup co-authored more than 20 articles, including 7 as principal contributors, in journals such as J. Biol. Chem (2), BMC Biol., Curr. Pharm. Des. (2), Cell Microbiology.

Assessment of the unit's academic reputation and appeal

This is a solid nationally recognized team and invested in. The team has attracted significant national and European funds for its drug discovery projects.

The team members are active in meetings (three times involvement in the organization of symposia, chair of sessions, seven invitations for presentations at international symposia), an editorial board (Molecular and Biochemical Parasitology), evaluation panels (for the "Direction Générale de la Recherche et l'Innovation", the French Foreign Office to participate in site visits in Asia and the Middle East, the ANR, and the AERES), etc… Both subgroups have a good international visibility through activities such as participation of the schistosome genome sequencing project, framework programs of the European Commission, drug development projects. Most of the invited conferences are for the senior scientists of the S. mansoni subgroup, raising concern for the impact of their impending retirement on the visibility and attractiveness of the team.

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

The team does the usual activities in interaction with the public by the standards of the CIIL: outreach sounds good with the participation in the school programs and open days. The web site does need a total revamp with accessibiity to the general public, a key issue for rendering the team visible from outside. The team interacts with the economic environment via partnership with two Swedish small and medium enterprises (SME), Kancera and Adlego, in the frame of its EC-funded projects.

Assessment of the unit's organization and life

The team is quite large, but essentially composed of two subgroups, with little real overlap aside from the drug screening. The PARADDISE award is significant and constitutes a lifeline for this grouping.

The ratio of permanent staff compared to the number of PhD students and post-doctorants is on the high side, in particular as a result of the absence of post-doctorants, and the number of young scientists is low. It should be possible to attract more (young) scientists, in particular from other countries.

Assessment of the unit's involvement in training through research

Staff members are involved in teaching at the university. In addition, seven PhD theses have been defended in the past five years. Five thesis projects are currently ongoing in the team, which also hosts seven Master students. However, there seems room (and need) for extending training through research to post-doctorants.

Assessment of the strategy and the five-year plan

The strategy of the team for the next term is to continue the characterization of the molecular events controlling the growth and differentiation of the parasites S. mansoni and P. falciparum, focusing on histone acetyl transferases and tyrosine kinases (S. mansoni) and phosphatases (P. falciparum). It is not clear whether the proposed synergy between phosphorylation and HDACs (and other histone modifying enzymes) is well made. These are very different classes of enzymes, and as a result they require distinct lines of investigation. This dichotomy represents a major challenge for the future plans of the team. Similarly, the cell signaling interests in the two subgroups are very distinct and different from one another. The two parasites studied in this team present different problems from the point of view of reverse genetics that are most obviously solved for Plasmodium. The group leader was very uncertain of the background when questioned on these issues.

There are plans for better integration of the two subgroups, by focusing on themes involving both parasites (e.g. phosphorylation/dephosphorylation). However, the future of the Schistosoma group is uncertain because of the retirement of two senior members in the near future.

Conclusion

The twin focus on schistosomes and malaria parasites has the hallmark of a marriage of convenience held together simply by the drug screening funded by the EC project PARADDISE – other sources of funding are not obvious. This is relatively weak grouping going forward in need of support and management. A clear strategy has to be made for the group in the future. Options include (i) finding a new *Schistosoma* sub-group leader, (ii) recruiting a malaria biologist with strong potential to assist the current leader ; (iii) stop one of the themes to focus on a single model, otherwise the perenity of the team in its actual shape would be weakened.

- **Strengths and opportunities:**

- the strong background of the team on two important parasites and their life cycles opens possibilities for cross-fertilization;
- the impending retirement of two senior researchers offers possibilities to rededicate or invest in youth, by recruiting a high profile candidate to conduct the challenging program proposed by the team.

- **Weaknesses and threats:**

- the plan to work on two parasites with very different life cycles is a potential source of dispersion and dilution of resources;
- the two schistosome leaders will retire within 5 years and it is not clear at present if and how they will be replaced;
- there is limited reverse genetics in the parasites studied, either because of technical limitations or through intractability;

- **Recommendations:**

The succession problem for the schistosome leaders must be solved as soon as possible. The reorientation of some projects must be considered: in particular, a strategic choice to focus solely on P. falciparum or not must be made.

Team 3: Plague and Yersinia pestis (PYP)

Name of team leader: Mr Florent SEBBANE

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)	2	2
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	4	
Theses defended	3	
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	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The team, created with the new leadership in 2008, has taken up the Yersinia projects conducted previously in the laboratory, with the objective to decipher the virulence of Yersinia pestis and its dissemination. Another objective of the team is to gain knowledge on the molecular mechanisms associated with *Y.* pestis pathogenicity, in order to propose new therapeutic strategies. This is an important issue, as there is no current efficient protection against pestis, if provoked by pan-resistant strains. The team developed a highly original flea model of infection/ transmission of *Y.* pestis, which required establishment of a NSB3 insectarium. The facility and experimental system is now functional and represents a real opportunity for the future. The know-how and expertise of the team, which is quite unique worldwide, should have a significant impact on the quality of future publications.

In the last period, the team published 17 papers on Yersinia, including one in PLOS One, one in "Infection and Immunity" and one in "Journal of Infectious Diseases". Among those, 8 were signed as first or last author by members of the team. Members of the team also wrote three book chapters, and participated to other publications in collaboration (not related to Yersinia; 7 in total).

The team developed collaborations within CIIL with three teams, and two joint publications have already appeared in press.

Assessment of the unit's academic reputation and appeal

The team obtained grants in the last period but which ended in 2011 and 2013 from ANR and ERDF/ARC.

The team is still young and needs to be recognized at the national and international levels. It already succeeded in attracting several PhD students. However, due to actual lack of funding, no post-doctoral fellows were recruited in the team during the past 4-year period.

Because of the attractiveness of the flea-bacterial model, the team has contacts with several US laboratories with whom it plans to collaborate, pending obtention of funding. Things look promising and one International Travel Award was already obtained.

The emerging reputation of the team is attested by four international invited lectures in Finland, Norway, Singapore and the USA. The efforts towards international and national applications should be maintained. Collaborative projects, relying on the expertise of the team (flea model), will bring further attractiveness to the team.

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

One interview on TV, participation to high-school projects, involvement in the BIOTOX biosecurity exercise have to be mentioned in 2011 and 2012.

The team provides expertise on biosafety and biosecurity issues regarding putative terrorist attacks. Possible patent application is envisioned.

Assessment of the unit's organization and life

The PYP team was created in 2010, and comprises 9 people. It is structured in three subgroups, working respectively on plague pathogenesis, flea-borne transmission and therapeutics. The PI supervises the three subgroups and the interactions within the team seem to function. The PI has a lot of responsibilities, and may be helped more by other researchers, notably concerning supervision of students (one more HDR in the team would be welcome). Three new members joined the team in the last 4 year period (1 lecturer, 1 research engineer, 1 technician).

Assessment of the unit's involvement in training through research

3 PhD thesis were defended since 2008, and 2 are ongoing in the team, all under the supervision of the PI. Three team members participate in teaching and/or are responsible for Master modules or dispense Microbiology courses (60h/year) at the Lille university. The team also built on its research experience to set up the first university diploma in Biosafety/Biosecurity and the PI built a Microbiology Diploma.

Assessment of the strategy and the five-year plan

The projects are based on the accumulated knowledge and the know-how of the team on Y. pestis, with highly interesting developments in the flea model. The long term goal is to develop systems biology approaches to study the interaction between Y. pestis and the flea vector. The strategy is very original and ambitious.

Several other directions have been presented (e.g. per-pool screening of mutants; assignment of functions to identified genes) and the team plans to collaborate with eight groups at six different institutions. While all these projects are ambitious, they are somehow disconnected. Given the small size of the group, the most advanced and promising projects, such as setting up an automated screening in the flea model, should be chosen as priority, in order to be competitive.

One priority for the next five years will be to secure financial support through grant applications, to complement the institutional funding currently allocated by CIIL to the team.

Conclusion

This is a young and dynamic team, developing very original novel projects focusing on Y. pestis, and led by a PI with a strong expertise in the flea stage of the infection. The production in terms of publications has been modest in the past years, in large part due to the important investment in time and resources required for the establishment of an insectarium enabling to study the flea-borne stage of the Y. pestis infectious cycle. The perspectives for this team are excellent since it is supported.

- **Strengths and opportunities:**

The establishment of an NSB3 insectarium within CIIL provides the team with the opportunity to develop the flea model for Y. pestis infections. This is a unique place in Europe to conduct this kind of research. The team has interesting collaborations with other teams at CIIL, and several contacts with laboratories in the USA, which attest of its potential. Common grant applications should be the priority.

- **Weaknesses and threats:**

The team is still “young” and is building up to achieve recognition in the field.

There is a lack of financial support, other than institutional funding.

- **Recommendations:**

The committee suggests putting major efforts on projects that are linked to the flea model of infection. The collaborative projects within the institute should be maintained.

Contacts with US laboratories are precious and will be decisive for the future. Exchange of students and/or creation of a LIA may be envisaged to reinforce and formalize these strategically important interactions.

Team 4: Bacterial Respiratory Infections, Pertussis and Tuberculosis (BRIPT)

Name of team leader: Mr Camille LOCHT

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	9	9
N3: Other permanent staff (without research duties)	6	7
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	5
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	20	21

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	6	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	5	5

• Detailed assessments

Assessment of scientific quality and outputs

The scientific production is excellent, with more than 100 papers published in the last 5 years, and several articles in high impact journals (Nat Med 2009, PNAS 2010, NAR 2011, Nat Genet 2013). The team also applied for several patents, some of which have been licensed to industry. One hallmark of the team BRIPT is a strong involvement in basic but also translational research on B. pertussis and M. tuberculosis. For example, basic research on B. pertussis has led to the development of a live vaccine that has entered clinical trial. In addition, molecular and genetic study of M. tuberculosis has led to the development of a kit for molecular typing; the technology has been made widely popular through numerous training courses and is now recognized as a gold-standard by the american CDC. Study on M. tuberculosis HBHA antigen has led to important discovery and development in terms of latency detection and vaccination. Novel compounds have been identified to boost current therapy against tuberculosis.

Assessment of the unit's academic reputation and appeal

The senior members of the team are involved in a number of research consortia (including FP6 and FP7 EU projects, one of them being coordinated by the team leader), and invited to numerous (more than 100 for the previous period) national and international meetings and conferences, on all continents. The visibility and reputation are excellent. The team is attractive, with 5 PhD theses defended, 2 current PhD students, and 4 post-doctorants. Several team members are consultants or experts for national and international funding bodies or public health survey agencies (ANR, CDC, WHO, and a number of others).

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

The team has strong contacts with industry, and is very active in innovation. 9 patents were granted to the team, two of which have been licensed. The team members are strongly involved in communication to the public (public conferences, TV programs, interviews in the press, etc).

Assessment of the unit's organization and life

The team is composed of 22 people, with a nice repartition between permanent staff (7 research scientists and 5 engineers or technicians) and trainees (6 post-doctoral fellows and 3 PhD students). It is structured in three subgroups dedicating their efforts to three complementary themes: bacterial envelope, genomics and genetic regulation, vaccine development.

Assessment of the unit's involvement in training through research

5 PhD students graduated during the review period, 2 PhD students are currently trained. The team also trained two US summer students sponsored by the HHMI since 2010. The team members are deeply involved in training through research, and also actively participate in Master classes in France and Belgium. In addition, the team has organized more than 20 training courses, on national and international levels.

Assessment of the strategy and the five-year plan

The project is ambitious and in line with previous achievements, with multiple basic and translational developments in the fields of B. pertussis and M. tuberculosis research (diagnostics, treatment, vaccines). The project aims at: (i) better understanding the structure of B. pertussis haemagglutinin FhaC ; (ii) better understanding Mtb HBHA secretion using a variety of unbiased and candidate-based approaches ; (iii) completing the analysis of the structure/function relationship of the two-component system partner BvgS ; (iv) deciphering the molecular evolution of Mtb, from M. prototuberculosis to Mtb using innovative in vivo experimental evolution approaches ; (v) developing further B. pertussis and Mtb vaccine candidates. The team has the capacity to conduct these projects.

Conclusion

The team is clearly a leader of international repute in the fields of B. pertussis and M. tuberculosis research.

- **Strengths and opportunities:**

- the team members are deeply embedded in national and international consortia, with strong connections with european and US partners;
- the scientific production is outstanding;
- innovation and interaction with the economic world is outstanding;
- the team has a strong visibility.

- **Weaknesses and threats:**

More PhD students should be hired, and more funding for the coming 5 years should be raised, in order to secure the team's research activities.

- **Recommendations:**

The excellent international visibility of the team, and its strong interconnection with the national and international academic and private sectors, should be exploited to raise more funding (e.g. ERC).

Team 5: Cellular Microbiology and Physics of Infection (CMPI)

Name of team leader: Mr Frank LAFONT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	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	**3**	**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	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

This small team focuses on the cellular, molecular and biophysical aspects of host-pathogen interactions, with a particular interest in the interaction of intracellular bacteria (Shigella flexneri, Listeria monocytogenes, Yersinia pseudotuberculosis) with cellular membranes. In the past 5 years, it made important contributions on the role of autophagy in the control of intracellular bacterial infections (e.g. the neutralization by autophagy of molecules that can be sensed by the cell as danger signals, identification of autophagosomes as a site of replication for Y. pseudotuberculosis). The team also contributed important technical innovations in cell biology to uncouple pathogen adhesion and entry, and to investigate the role of membrane elasticity in cell signaling. The team has published 19 articles on the period, including 3 in Cell Host & Microbes. 10 articles are signed as last author by the PI. Several articles are the results of collaboration with leading experts in microbiology.

Assessment of the unit's academic reputation and appeal

The PI gave 30 invited talks in France or abroad on all continents, including prestigious conferences such as Gordon conferences (twice) or EMBO conferences (twice). The academic reputation of the team is also asserted by the fact that the PI has acted as an expert for foreign bodies during the past five years (e.g. Welcome Trust), and is serving on the editorial board of three cell biology or microbiology journals. The CMPI team has established a cutting edge technological platform and many leaders in the field of infectiology are eager to collaborate with the PI. The PI of the CMPI team is also the scientific director of the Bioimaging center of Lille, which leads the Equipex ImagInEx Biomed (14M€). The team also participated to 5 ANR grants, including 2 as coordinator.

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

The CPMI team has a strong commitment for popularization of science. The PI initiated and coordinates the « kids campus » of Pasteur Institute, which involved a total of 2400 children at the national level since its creation in 2007. He also initiated the « Apprench'ti chercheur » in 2010 and the « Apprench'ti journalistes scientifiques » in 2013 for high-school students.

Another remarkable facet of the CPMI team are the numerous contracts with industry, often with world leaders (Zeiss, l'Oréal, Veeco/Bruker) for a total over 1,6M€.

Assessment of the unit's organization and life

The team is composed of two permanent researchers, one technician, one or two post-doctoral fellows and two PhD students.

Assessment of the unit's involvement in training through research

3 PhD thesis have been defended in the team since 2008, and a fourth one is ongoing. The PI of the team is responsible of teaching units at the Master and Doctoral levels, on Cell Physics and Scientific Transmission, and is a co-organizer of the M2R program in host-pathogen interactions. He is also a coordinator of an inter-university degree in Cellular Microbiology between the universities of Lille and Paris VI. The CMPI team has also organized or participated to summer schools in France and abroad (EMBO course, atelier INSERM).

Assessment of the strategy and the five-year plan

The team intends to build on the tools and expertise acquired in the past years to tackle three ambitious questions pertaining to bacteria-cell interactions. The first is the role of autophagy in the control of bacterial infections ; the second is the physical dissociation of membrane signaling at the cell surface, upon binding of the bacteria, and during entry ; the third is the impact of the mechanical properties of the membrane (elasticity vs stiffness) on signaling.

The scientific strategy is somehow hard to decipher on the written document, and was not totally clarified during the discussions. There is no proposal to solve a precise biological question, and the strategy seems to be mainly driven by collaborations, with scientific questions brought forward by groups soliciting the scientific and technical expertise of the team.

Conclusion

The team is developing innovative technological approaches to study the interaction of intracellular bacteria with cellular membranes. Its production in the past five years and its international visibility are excellent.

- **Strengths and opportunities:**

The CMPI team has established a cutting edge platform in imaging, as well as strong connections with other teams of CIIL and some of the world leaders in infectiology. The team has a strong transdisciplinary approach, associating physics and biology, which represents another key asset to develop highly innovative approaches in the study of host-pathogen interactions. The strong interactions with industry will help perpetuate improvement of the imaging platform.

- **Weaknesses and threats:**

The small size of the team is seen as a threat, especially in light of the many other activities of the PI (including preparation of a degree in management). Given its international recognition, it should be possible for the PI to attract more funding, including salaries for post-doctoral fellows. The lack of clear objectives for the next five years is also a reason for concern.

- **Recommendations:**

The CPMI team should decide on clear objectives, set priorities among them and obtain resources, in terms of both financial support and lab space, to attain them.

Team 6: Molecular & Cellular Virology of Hepatitis C (MCVHC)

Name of team leader: Mr Jean DUBUISSON

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		1
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)	6	6
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	14	15

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

• Detailed assessments

Assessment of scientific quality and outputs

The MCV-HC team (starting in 1994) was firstly identified in 2001 as the independent research unit UPR2511 by the CNRS. In 2006, MCV-HC was secondly associated with another unit to create the Cancer unit UMR 8161. In 2010, MCV-HC decided to participate in the creation of the CIIL unit on the campus of the Pasteur Institute of Lille. Since 2008, investigators of MCV-HC have a basic research interest on interactions between Hepatitis C virus (HCV) and host factors at the molecular and cellular levels. The MCV-HC research program was geared towards (1) a comprehensive study of the functions of HCV glycoproteins in virus entry and assembly, (2) the role of lipid-associated receptor in virus life cycle, (3) the identification of cellular factors playing a crucial role in HCV replication, (4) the development of antiviral agents against HCV, and (5) understanding the role of non-structural proteins in the morphogenesis of HCV. The published works by the MCV-HC team (43 with IF from 3 to 12, including PLoS Pathogens, Hepatology (3), J. Virol. (10), J Biol. Chem. (8)) are of excellent quality at the international level and they have allowed to improve knowledge on the biology of HCV.

Assessment of the unit's academic reputation and appeal

MCV-HC team is internationally recognized in the field of basic research on HCV and it has made several major contributions in this area. The MCV-HC's PI (H index 47), who was awarded the Silver Medal of CNRS in 2003 and then received the prestigious International Scholar of the American Foundation HHMI (2005-11), has a long and productive record in academic virology, particularly in the investigation of the mechanisms of HCV entry. MCV-HC has contributed to the creation of the National Network on Viral Hepatitis which is supported by ANRS. The MCV-HC team hosts students (master and PhD levels) as well as post-doctoral fellows originated from different countries including the USA. Most of its former students now pursue a career in academic research. The investigators of MCV-HC have established fruitful collaborations that have been mostly supported by research grants within France (CNRS, FRM, ANR and mainly ANRS grants) and then, in a second rank, within Europe (Marie Curie grants), and abroad (HHMI grant). Although the MCV-HC has finally been little represented within the different EU FP-7-Health programs since 2008, the team is now funded with a new ERA-NET program. The team has recently filed two patent applications in the area of HCV antivirals/ inhibitors of HCV entry.

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

MCV-HC team supervises high school students during a short internship in research lab. The investigators of MCV-HC have deposited important patents in the field of antiviral agents against HCV. The introduction of solid partnerships with SME working on the development of antiviral compounds could be of great interest for MCV-HC in the next five years.

Assessment of the unit's organization and life

The MCV-HC team currently encompasses in the addition to the PI (DR1, CNRS), senior researchers from CNRS (two DR2, two CR1, and one CR2) and one MCU-PH from University Lille 2, research engineers (3) and technicians (3) from IPL, INSERM and CNRS, post-doc fellows (2), PhD students (4), and master 2 student (1). The MCV-HC team is composed of three subgroups "functional studies of HCV envelope proteins" (headed by the team leader), " replication and assembly of HCV" (headed by two CNRS-DR2), and " cellular aspects of HCV " (headed by one CNRS-CR1). Such rational organization is greatly beneficial at the light of the scientific production as well as international academic reputation of MCV-HC.

Assessment of the unit's involvement in training through research

The MCV-HC team contributes to teaching activities for Master 2 and has participated in a EU ITN between 2006-10. On the period 2008-13, the team trained 3 students for a technician degree, 5 students for a Master 2 thesis, and 8 for a PhD thesis. Also, 15 foreign students or scientists were hosted by MCV-HC for internships. The MCV-HC team is clearly identified as an attractive virology laboratory for students and postdoctoral fellows who are interested in working on HCV.

Assessment of the strategy and the five-year plan

The intention of MCV-HC team is to continue the current studies with a particular focus on the molecular basis of HCV replication. Towards this purpose, the MCV-HC investigators propose to understand (1) the role of lipid metabolism in the different stages of HCV replication (mainly entry, replication, assembly) through the use of available cell culture systems allowing virus growth, and (2) the mechanisms of HCV resistance to neutralizing antibodies with a final objective that would be to design new therapeutics including a prophylatic vaccine. The screens appear limited to the entry and assembly steps of the viral cycle, and the team could be more ambitious and develop broader screens.

It is also proposed to implement a new project on the biology of human respiratory coronaviruses with a particular focus on emerging MERS-CoV, a promising but very competitive field. The rationale for this choice is based on (i) the scientific and medical background of two MCV-HC's research assistants on SARS-CoV and MERS-CoV ; and (ii) the general activities of the team about HCV assembly and production of molecular clones derived from RNA viruses. Given that only two junior investigators could be directed towards a new project on coronavirus, it may be questioned if the human resources devoted to this highly competitive program are sufficient.

Conclusion

The future projects of MCV-HC team are mainly based on exploiting previous results on HCV and only two research assistants are foreseen to take over a new project on MERS-CoV. Over the next couple of years, the distribution of the efforts between these two major topics in virology should be more equilibrated. A particular effort should be done for securing funding on the future projects of the team MCV-HC, with a particular attention on coronavirus topic for the next five years.

- **Strengths and opportunities:**

The PI and the investigators of MCV-HC are internationally recognized in the highly competitive field of HCV. They succeeded in attracting a number of national and international grants and others, PhD students, post-doctoral fellows and research assistants. The management of the team by the PI has been achieved in a successful manner thereby leading to an excellent scientific production and international academic reputation of MCV-HC. The implementation of a future project on MERS-CoV does open the virological niche usually occupied by the MCV-HC team since its creation and also represents an opportunity for CIIL.

- **Weaknesses and threats:**

The securing of research funding for the next five years should be a priority by relying on new EU-FP7 Health 2020 programs and also through partnerships with companies (SME) involved in the field of antiviral compounds. Because MERS-CoV is a very competitive topic, the introduction of active collaboration with scientific community working in this field should be established without delay.

- **Recommendations:**

The future project on MERS-CoV is an opportunity for opening the viral niche occupied by the MCV-HC team since its creation. A particular attention will be made on the repartition of efforts between HCV and MERS-CoV groups. The securing of research funding for the next five years must be ensured with a particular emphasis on human respiratory virus projects. Active collaborations with international academic groups that are recognized in the field of human coronaviruses should be promptly initiated by the MCV-HC team. Also, an effort should be made to profit from patent exploitation and establish closer links with Industry in the area of HCV therapeutics.

Team 7: Nods-like receptors in infection and immunity (NLRII)

Name of team leader: Mr Mathias CHAMAILLARD

Workforce

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

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

• Detailed assessments

Assessment of scientific quality and outputs

The team NLRII studies the role of cytosolic surveillance mechanisms in the regulation of intestinal inflammation and immunity. The team has been extremely productive, especially in light of its youth and its relative small size. It has yielded numerous publications (40), including 7 in very visible journals (JCI, PNAS, Gut), which have already attracted a significant number of citations (52 for the NLRP6 PNAS 2011 paper; 41 for the PPARgamma 2010 PNAS paper; 20 for the REG3beta 2009 GUT paper and already 10 citations of the 2013 JCI paper).

Assessment of the unit's academic reputation and appeal

Relative to its age, the team has an outstanding academic reputation and appeal. The team has been granted the "FRM label" twice in a row. The PI has been invited in 30 national and international conferences, he has been chair and/or main organizer of international meetings and he is a member of the international inflammatory bowel disease genetic consortium. The group has attracted 5 post-doctorants (including 3 from abroad).

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

The team has been successful in attracting competitive grants with the team leader as a PI (2 FRM label, one large ANR consortium) or as a partner (One Equipex). The PI has been or is a member of national scientific evaluation committees (INSERM, APHP).

Assessment of the unit's organization and life

The team is very dynamic and heavily relies on rotating (Master) and PhD students as well as on post-doctoral fellows.

Assessment of the unit's involvement in training through research

The team has trained 2 PhD students and a very high number of rotating students (5 M2, 10 M1). The PI of the team exerts teaching responsibilities for a degree on Infectious Diseases in Paris and for the Master 2 « Biologie Santé » in Lille.

Assessment of the strategy and the five-year plan

The team works on a trendy topic and has been quite successful and productive using available tools. The team is now engaged in generating new tools (tissue-specific NOD2 and NLRP6 KO/KI models) and approaches (mouse gnotobiology) to tackle important questions related to Nod-Like Receptors (NLRs) biology and their impact on intestinal symbiosis. These questions include how NLRs shape intestinal symbiotic communities and how NLRs activity ensures community stability. The proposed work on the modulation of the microbiota composition through the use of novel probiotic strains, although obviously very risky, is extremely promising.

The strategy of the team has evolved between the submission of the written document and the site visit, as a result of the obtention of new funding.

Conclusion

This is an excellent start for a young group. The team works in a very competitive field and has been very productive and successful in securing major fundings and productive collaborations. The strategies for the coming year will have to be closely managed by the PI and should rely on the technological assets that the team is currently developing to maintain their position at the leading edge of the field.

- **Strengths and opportunities:**

The team works on a hot topic and is already very visible in this competitive field. In addition, the group is gathering a collection of innovative tools and technologies, which will be instrumental for their future research plans to stay at the frontlines of the field.

- **Weaknesses and threats:**

The overall lab strategy is not always very clear and seems to rely on opportunities. Also, the relative modest size of the gnotobiology set-up as well as the anaerobic bacteria culture /manipulation potential of the team is seen as a potential threat.

- **Recommendations:**

This is an excellent start for a young team. The committee recommends paying attention to the overall strategy of the group and to build on the innovative assets that the lab has developed. The team is strongly encouraged to develop its own expertise in bacteriology and gnotobiology.

Team 8: Lung Infection and Innate Immunity (LIII)

Name of team leader: Mr François TROTTEIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	5	7
N3: Other permanent staff (without research duties)	5	5
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	14	15

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

• Detailed assessments

Assessment of scientific quality and outputs

This is a very well balanced research team (currently strong of 22 people), which is broadly composed of 3 different arms (a- NKT cells during respiratory infections, animated by the team leader ; b- Early immune response to adjuvants and infections, animated by an INSERM DR2 ; c- Respiratory Infection and Chronic Inflammation, animated by an INSERM CR1). The 3 subgroups made important contributions to the overall output of the team, with a special mention for subgroups a) and b).

The overall objective of the team LIII is to investigate the role of innate immunity in host defences and pulmonary pathogenesis during respiratory infections. Broadly, three different themes have been tackled in the previous period.

Theme 1 (Innate immune responses to respiratory infections) has concentrated mainly on the role of NKT cells in experimental influenza A virus (IAV) and *S. pneumoniae* infections in murine models. Important and original findings include the demonstration that NKT cells produce IL-22 that protects against epithelial damage caused by IAV. This has yielded a patent application for future potential therapeutic benefit. The role of the newly identified innate immune lymphoid cells has also been studied in that context, attesting of the reactivity of the team.

Theme 2 tackles an important issue, namely secondary bacterial infections, post-influenza. These can be devastating, as remarkably demonstrated during the 1918 Spanish flu. Important findings by the team have centered on the role of IL-22 in repair and IL-10 in limiting bacterial super-infections.

Theme 3 also addresses an important question, the mode of action and optimization of adjuvants, mainly flagellin and the iNKT cell activator α-GalCer. The data obtained have also led to a US patent application.

The team as a whole has published 87 peer-reviewed articles (including 30 as main contributors) in journals with an IF between 4 and 7 such as J. Immunol., J. Infect. Dis., J. Virol., Mucosal Immunol. In addition, 6 patent applications are under evaluation, 2 patents have been granted and a third one has already been licenced.

Assessment of the unit's academic reputation and appeal

The team is attracting a fair number of foreign students and post-doctoral fellows. For example, fellows and students have been recruited from India, Mexico, and South America. Altogether, 9 post-doctorants have been appointed since 2008.

The team has obtained very significant funds through national and international highly competitive calls (INCa, ANRS…) and a significant numbers of these include collaborative international networks training, Network Initiative FP7 (2013-16), ECOS-Sud (2009-11) and INSERM-CONICET (2009-11, 2013-15).

In addition, members of the team are regularly invited to national and international conferences, including for the last period a Keystone conference and the annual meeting of the American Society for Microbiology. Many talks were also presented at international conferences as selected abstracts.

The expertise of the team has also been requested by a variety of national and international agencies (ANR, ANSES, INCa, FRM, DIM, VMC, EEC, Wellcome Trust…) to evaluate grant applications, which attests of a clear national and international appeal and attractiveness.

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

The dissemination of science to the general public by the team LIII encompasses organization and teaching in public conferences (e.g. '5 à 7' COPD conference, 'fête de la science', 'nuit des chercheurs'). Maybe more prominent than the latter is the involvement of the team in local, regional, and national academic scientific administrative tasks. These involve participation in CIIL, University Lille, COMESP Pasteur Institute-Paris, and IFR scientific council committees. Notably, the team leader will be the new elected Deputy Director of the CIIL and one member of the team will be the director of the 'Federative Research Structure-SFR Maladies Infectieuses, Inflammatoires et Immunologiques (a 320 people-strong organization).

Assessment of the unit's organisation and life

LIII is a large research team, currently strong of 22 people, including 14 permanent/post-doctoral positions and 8 PhD students. The team is broadly structured in 3 subgroups, developing 3 distinct themes. The structure of team is well balanced, and each of the 3 subgroups made important contributions to the overall output of the team. People seem to interact well within the team LIII, and responsibilities are shared between the different staff scientists in an interactive fashion.

Assessment of the unit's involvement in training through research

Since 2008, the team has trained 22 L3 and M1 students (for short periods of time).

In addition, 7 PhD students and 17 M2 students have been trained during that period. Some of these students have subsequently been hired as post-doctorants in important laboratories abroad, in Belgium, the US, and Australia. Currently, 7 PhD students are in the unit. This important turn-over is probably made possible by the strong presence of two PIs, as well as one MCF in the PhD students selecting committees at the University. The latter was a member of the section 87 of the CNU and was therefore involved, at the national level, in the hiring and nurturing of young researchers. Notably, one PI will now be responsible for the organization of the new M2 training program (Infection, Inflammation, Immunology, 2015-2019).

Assessment of the strategy and the five-year plan

The balance between the different sub-groups in this team is set to be well preserved for the next term, with all having important roles in driving the different research themes. One of the weaknesses of the previous term may have been the relative lack of clinicians in day to day research activities. This is set to change, with the involvement of 3 MDs, who will join the team and will be active at the bench. Some are already registered for a PhD, and this should insure for improved translational research activities.

The program for the following 5 years will build upon the existing themes, which are already well established (Role of the Th17-Th22 axis in host defenses during influenza and *S.* pneumoniae infections ; Role of adjuvants (flagellin, α-GalCer) against respiratory infections) and important developments are to be expected, especially through the studies of potential synergies between immune adjuvants and antibiotics, and the importance of vaccination (eg against *S.* pneumoniae and NTHI) in 'COPD mice' and patients.

Importantly, the role of cell types less studied in that context (ILC3 and CD3 bright γδ T cells) will be further examined, and an important extension of these studies will be considered, with the arrival of a newly appointed DR CNRS. This PI will bring in the team new expertise on the role of obesity in worsening inflammatory conditions, through the association of dyslipidemia and gut dysbiosis. This will be studied mainly in COPD 'smoking murine models' that the team has established locally in Lille. During the following term, the link between obesity, susceptibility to respiratory infections and COPD will be studied in humans, through already obtained funding (bourses de Région Nord/Pas de Calais).

Conclusion

During the last 5 years, this team has made excellent progress on the deciphering of the role of innate immunity in host defenses and pulmonary pathogenesis during respiratory infections. The scientific output of the team in terms of published articles and materials is excellent, and it is attracting a fair number of foreign students and post-doctoral fellows. In addition, the team has obtained very significant funds through national and international highly competitive calls, and its interface with the public is also noteworthy.

- **Strengths and opportunities:**

This a well balanced team, with strong expertise in particular in microbiology, immunology, and respiratory infection and chronic inflammation. All the sub-groups seem to interact well and synergies are obvious in terms of the publication record (87 peer-reviewed articles from 2008, including 30 as PIs). This is a team with an obvious interest in translational approaches, as evidenced by their growing links with clinical medicine, and the important number of filed patents (7), including an industrial license. The arrival of 3 clinicians in the team, as well as that of an established DR with an interest in metabolics and inflammation should further strengthen this expanding group of researchers.

- **Weaknesses and threats:**

The team has to build up optimal synergies with other investigators, a point that the team is currently performing.

- **Recommendations:**

An effort could be made to try to publish in high-impact general journals. Some of the projects most certainly will yield results that may be published in such journals if pushed to a further level of analysis.

Team 9: Lactic Acid Bacteria and Mucosal Immunity (LABMI)

Name of team leader: Mr Bruno POT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	3	3
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**9**	**9**

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

• Detailed assessments

Assessment of scientific quality and outputs

The team Lactic acid bacteria and mucosal immunity studies a historical topic in host/microbe interaction that has been neglected for many years and is now being "rediscovered", i.e the probiotic potential to intervene on microbiome-related disease. This team has a long lasting and recognized expertise in studying lactic acid bacteria in the context of probiotic application, and has also been really performant over the years in developing tools (recombinant LAB strains) in this field.

After studying the diversity of LAB strains activity on biological read-outs, the team has focused its attention on studying the anti-inflammatory potential of LAB strains. It has now revealed a mechanism underlying such effects. The team has been successful in identifying other strains with such capacities and it is collecting exciting results on the mechanisms underlying other biological effect of probiotics related to diet induced obesity (unpublished).

The scientific production of the team relative to its size has been very good to excellent in its quantity, quality and regularity (38 research papers during the period, 11 with lead authors from the team). Articles were published in Gut (IF >10; 4 articles), Allergy (IF 5,9), Vaccine (IF:3,76), Int. J. Food Microbiol. (IF:3,327). Four articles have already been cited more than 16 times, and one of them more than 37 times since 2011. The team has also contributed 11 reviews and 10 book chapters.

Assessment of the unit's academic reputation and appeal

Based on its long lasting and recognized expertise in studying lactic acid bacteria, the PI of the team as well as another senior member of the team have been invited in numerous conferences (presenters or chair), scientific boards and panels (71 in total including, apart scientific conferences, AERES, INRA ALIMH/MICA, INRA recruitment board, National probiotic network) demonstrating an excellent academic reputation.

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

The team is extremely proactive in establishing connections with the social, economic and cultural environment, and has an outstanding track-record of contracts with private companies (worth around 1M€). The PI is also actively communicating to the public on the potential of using probiotics in microbiome-related diseases (press conferences, interviews, posting videos on internet, lay people presentations, setting up and reviewing websites contents for the larger audience).

Assessment of the unit's organization and life

The team is well organized and stable despite the loss of a technical staff during the period, but the productivity of the group would profit from hiring more PhD students and focusing resources on less projects.

Assessment of the unit's involvement in training through research

Related to the above comments, the team should invest more efforts in training master and PhD students given the number of HDRs but it should be noted that the outreach activity (see above) of the team significantly compensates this lack of training through research. One PhD student graduated during the past term.

Assessment of the strategy and the five-year plan

The proposed project for the next five years focuses on identifying new probiotic strains beyond Lactic Acid Bacteria (LAB) and clarifying the mechanisms of health-promoting properties of some established probiotic LAB strains. The project is well thought, very clear, balanced (containing basic, applied and translational aspects). Overall, it has high potential for new discoveries. Notably, understanding the mechanistics of probiotics will be essential for future applied research. Thus the results from the ANR project application "ALIA-Surfing", which aims at identifying genes/candidates will be crucial for future work. The project of the team is an elegant mixture of productive approaches relying on the strength of the team and past discoveries (recombinant LAB projects, probing biological effect of LAB strains, and the PGN project) as well as on more risky and novel approaches (anti-obesity and the autophagy projects) but those are already secured by exciting preliminary results.

Conclusion

The team LABMI, which is well positioned and recognized in the Lactic Acid Bacteria field, has been continuously developing tools and investing research efforts into fundamental and more applied research questions into the field of probiotics. The team has very good outputs in terms of publication and funding. It is also extremely proactive in linking its activity with the social, economic and cultural environment. The proposed research plan is excellent and has great potential for important discoveries.

- **Strengths and opportunities:**

The research of the team LABMI focuses on a subject, the use of Lactic Acid Bacteria (LAB) strain as probiotics, which carries a high potential for use in intervention strategies in microbiome-related pathologies. This potential is more and more recognized in the scientific community and yet challenged by the policy makers. As a consequence the field still needs to be substantiated by continuous delivery of experimental evidences of probiotics efficacy and with basic knowledge of the underlying mechanisms. Given its expertise, high visibility in the probiotic field and its strong links with the industry and emerging links with the clinics, this team is ideally placed to efficiently tackle those issues by developing the proposed original approaches ranging from basic research to the clinic.

- **Weaknesses and threats:**

However, the team is relatively small and there is a risk of dilution of the research efforts given the numerous collaborations with private partners planned or on-going. As a consequence the publication output of the team is very good and regular but lacks remarkable impact on those topics. Given the potential of the field, the mechanistic studies of the team will have much more impact, and should be strengthened. Another identified weakness is the relative poor investment of the team in training through research.

- **Recommendations:**

The committee would like to recommend to the team to invest more in basic research. Priority should be given to chasing the mechanisms underlying probiotic effects rather than continuing screening for new probiotics. It is important for the probiotic field that this basic research is performed by academic laboratories, as industry will not do it. As a consequence, the policy of the team for securing grants should be funneled toward this goal and allocation of the team resources should be thought accordingly. One way to invest more into basic research projects and to increase the manpower of the team is to train more students, which should be a priority for the team.

Team 10: Basic and Clinical Immunology of Parasitic Diseases (BCIPD)

Name of team leader: Ms Sylviane PIED

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

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

• Detailed assessments

Assessment of scientific quality and outputs

The team BCIPD is composed by two groups, one works in Malaria immunopathophysiology and the other in Clinical immunology of Schistosomiasis. Both groups combine generic clinical and fundamental studies in patients in India (malaria) and Senegal (malaria and schistosomiasis), and in experimental models.

Within these areas, the team has yielded, over the last 5 years, important contributions such as (i) Clinical trial Phase 3 of the vaccine candidate Bilhvax against urinary schistosomiasis; (ii) Identification of IgG autoantibodies to brain alpha2 Spectrin and Tububin B3 as biomarkers of cerebral malaria due to *Plasmodium falciparum*, and experiments to develop a diagnostic test to be used in endemic regions; (iii) study of the influence of environmental factors on children's immunity to vaccines (*Bordetella pertussis*) in Northern Senegal; (iv) Study of the temporal relationship between population genetics, immune response and their effect on protection of severe *P. falciparum* malaria in well characterized cohorts of patients in India; (v) Evaluation of Blastocystis infection in a cohort of Senegalese children.

These researches contributed to the publication of 34 articles, of which 19 as main contributors, during this period of which 50% had with IF in the range 3-10. However, the scientific production of the team is somehow limited, as for example only three articles were published in 2011, and none by the team leader. For the articles published by the team leader, the highest impact factor journal was J. Infect. Dis (IF: 5.9).

Assessment of the unit's academic reputation and appeal

This team is a clinical platform in Partnership between European and Developing Countries for clinical trials of new vaccine candidates. Although not directly related to the research of the team, this shows the strong implication of this team in field studies. The team is also coordinator of the Indo-French International Associated Laboratory CNRS-DBT on System Immunology and Genetics of Infectious Diseases (SIGID). SIGID is an operational network that combines clinicians and investigators in Parasitology, Immunology, Genetics, new Technologies, Advanced Informatics and Systems Biology approaches. The team organized several scientific international meetings in 2009, 2011 (2), 2012 (2), all abroad, in India or Africa. Altogether these data reveal the important involvement of the team and explain its attractiveness in this field for developing countries.

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

The team has contributed several initiatives towards public diffusion of science (TV debates), and education activities (participation in Women Health Education Program), in the improvement of health and sanitary of the populations involved in the trials. The team participated to the Conseil des ONG, and coordinated the Workshop on Infectious Diseases of the India-France Technology Summit.

Assessment of the unit's organization and life

The team is composed of 10 members (8 with permanent positions): 1 Assistant professor, 1 Prof Emeritus (25%), 3 researchers, 1 engineer and 1 clinical research assistant, 2 post-doctorantss and 1-2 PhD, and 1 administrative assistant (25%). The team is organized in two sub groups, one working on Malaria immunopathophysiology and the other on Clinical immunology of Schistosomiasis. The work of this team is complemented by the existence of an Insectarium. Both sub groups combine generic clinical and fundamental studies in patients in India (malaria) and Senegal (malaria and schistosomiasis), and in experimental models.

Assessment of the unit's involvement in training through research

Members of the team had teaching activities in five Master courses. The team is certified for PhD training (Universities of Lille 1 and 2, and University Pierre et Marie Curie, École Doctorale Biologie-Santé et Environment de l'Université Cheikh Anta Diop de Dakar, and UFR des Sciences de la Santé de l'Université Gaston Berger, Saint Louis Sénégal). 3 PhD thesis were defended, and 2 are ongoing. The team also trained 4 post-doctoral fellows, and organized two international courses on immunity and infection in India. The members of the team are members of the Directory Board of LabEx Parafrap PhD Program that begins in 2014. The Unit also coordinates the Indo French Integrated PhD Program, and created a Fellowship for Senegalese PhD and Master students.

Assessment of the strategy and the five-year plan

During the next CIIL mandate, the BCIPD team plans to continue its projects on the immunopathophysiology of malaria, and on clinical research and immunity in Africa. How the two themes will be associated and coordinated was not clear, either from the document or from the oral presentation, as a split between the Immunity and clinical research in Africa (ICRA) group, the EPLS Biomedical Research Center in Saint-Louis (Senegal) and the BCIPD team is announced.

The project Malaria Immunopathophysiology, led by the team leader will continue by trying to understand the mechanisms involved in the breaking of parasite tolerance observed in TLR 3 KO mice. This will be done by the study of B cell subsets activation and analysis of the antibody repertoires. The role of dendritic cells expressing TLR3 in the control of the *Plasmodium* yoelii infection will be analyzed. This work will then be applied to humans by investigating the association of TLR3 polymorphisms with severity of disease in cohorts of patients with P. falciparum infection. This will be achieved by sampling patients in India through SIGID program. This project will be supported by the LabEx Parafrap PhD program. Efforts will be made to identify factors involved in cerebral malaria by focusing on the role played by astrocytes and microglia interacting with P. falciparum and CD8 cells in the brain. This approach will be first developed in a murine model by sequencing chromosome 1 and 11 fragments of interest and analyzing transcripts before and after infection with P. berghei ANKA. This part of the project will be done in collaboration with team CMPI at CIIL. Also, the projects developed within the frame of the LIA SIGID and the LabEx Parafrap, which focuses on the study on several cohorts of P. falciparum infected patients recruited in a malaria endemic area of Orissa state (collaboration with Institute of Life Sciences, Bhubaneshwar city and SCB Medical College, Cuttack city) and in an urban malaria epidemic area in Gujarat state and Mumbai city (collaboration with Tata Institute of Fundamental Research, Mumbay) will continue.

The ICRA-EPLS project led by two other PI will investigate environmental factors that affect immunity searching for connections between the nutritional status, anaemia and schistosomiasis and the disruption in both nutritional biomarkers (including hormones such as leptin or Insulin growth-Factors) and inflammatory circulating components (such as CRP and IL-6). In the project named SANTINELLES, for "SANTé, INEgalités, viLLES" the team will address populations' health state in west African cities to understand the putative role of ecological and socioeconomic environments on major health public problems that strikes urban Senegalese population. Members of the ICRA-EPLS project will also be involved in the study of Schistosomiasis transmission control. This international collaborative program funded by Grand Challenge of Canada and Bill and Melinda Gates Foundation aims at the reduction of snail population by introducing their natural predator, the adapted prawn species Macrobrachium vollenhovenii.

Conclusion

Overall, given the strong expertise of the team, the technical feasibility of the proposed projects is very good when taken individually. However, the scope of the projects presented is very broad for a relatively small team.

- **Strengths and opportunities:**

- the major skill of the BCIPD team is its well-recognized expertise in parasite immunopathophysiology, both in human and experimental models associated;
- another major asset of the team is its strong involvement in field studies both in Africa and in India;
- the team has a strong involvement in teaching and specially in training, which is attractive for foreign students.

- **Weaknesses and threats:**

- the major weakness is the relatively small size of the team, especially regarding the important involvement in field work, which is highly time consuming. This is further evidenced by the low scientific production of some PI of the team in the last 5 years;
- the future organization and coordination of the projects is not clear, in particular with regards to the Immunity and clinical research in Africa projects.

- **Recommendation:**

The team should increase its size to provide full support to the ambitious and broad ongoing projects. This could be achieved either by recruiting additional permanent researchers or increasing the number of PhD/post-doctoral fellows trained in the team. Alternatively, decisions have to be taken regarding the priorities for the team, in order to focus the efforts on a smaller number of projects.

Team 11: Pulmonary Immunity (PI)

Name of team leader: Ms Anne TSICOPOULOS

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	5	5
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)	9	9
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	20	20

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	7	
Postdoctoral students having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	7	7

• Detailed assessments

Assessment of scientific quality and outputs

In 2010, the INSERM Unit U1019 became the team PI in CIIL. It is currently composed of 30 people including 5 permanent researchers, 11 clinicians, 6 PhD students and 4 M2 students. Activity of team PI focuses on the regulation of immune responses in two major respiratory diseases, sepsis with acute lung injury and asthma.

The main achievements during this last 5-years are 1) the elucidation of the role of endocan during sepsis, with the identification of a P14 fragment dramatically increased in patients with severe sepsis, while the non-cleaved form is associated with development of acute lung injury. The intellectual property associated with this major discovery led to the creation of a start-up company; 2) the first demonstration of the role of a chemokine as a differentiation factor able to induce Treg cells. This was a major breakthrough in the field of both chemokines and adaptive immunity.

Altogether, the team PI has contributed to the publication of 165 papers, with 42 plus 2 additional book chapters with first or last authorship for the members of the team. Of note, clinicians of team PI also participate in major clinical studies leading to publications in top medical journals such as the Lancet, JACI, Blood.

Assessment of the unit's academic reputation and appeal

Since 2010, the team PI has increased from 22 to 30 people. Although the number of invitations to international events is less than for some other teams, members of the team have participated to 55 invited conferences. In addition, the team has organized 12 meetings, including an annual international meeting gathering 2500 attendees, which contributes to its very good visibility.

Team members are active members of several French and International scientific network and committees, and their expertise is requested by several entities, such as ANR, AERES, British lung Foundation, Respiratory Health of Quebec.

Until now, the team PI was successful regarding the obtention of public and private fundings, accumulating a total of 2940 K€ in 5 years.

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

Diffusion of science to a non-scientific public is achieved through TV broadcasts, invitations to radio, and redaction of books for a wide readership, such as « le grand livre des allergies ».

In addition, data from the team have led to three patent applications and to the creation of a start-up company, LungInnov, in December 2009. Therefore, efforts of the team regarding this criterion are remarkable.

Assessment of the unit's organization and life

In 2013, the workforce is well balanced between these two research axis, with 10 people working on sepsis (3 researchers, 4 clinicians, 1 M2 and 2 PhD students), and 17 working on asthma (3 researchers, 7 clinicians, 1 post-doc, 4 PhD students, and 2 technicians, one of which will retire soon). People interact well within the team PI, but the team remains isolated from the other immunology groups within the CIIL.

Assessment of the unit's involvement in training through research

During the past period, the team has trained 8 L3, 14 M1 and 11 M2R students. In addition, 7 PhD students have defended their thesis (and obtained for some of them awards for their work) and 6 PhD thesis are currently on going. In addition, all the team members are involved in teaching at the medical school and the science University of Lille 1 & 2 at the master level (several courses in Immunology, Biology & Health, etc…). Team members also participate in other Master programs at different Universities. Some team members have teaching responsibilities such as coordination of a specialty in the Master 2 Research program of Lille 2 or chairing the examination board of the M2R Immunology.

Taken together this reflects a very good implication of the team to research through education.

Assessment of the strategy and the five-year plan

The current project of the team PI has been built on their previous findings, but will also focus on a novel axis i.e. the role of IL-33 secreted by endothelial cells in both sepsis and asthma. This is very original and the preliminary data are very promising. Regarding the theme 1, regulation of endocan expression and its putative protective role in sepsis will be assessed. Regarding the theme 2, the role of lymphoid cells (ILC) will be investigated in asthma, with their possible implication in pollutant-driven asthma exacerbations, and obesity-increased asthma. In addition, the role of ILC will be assessed in severe asthma for which there is currently no treatment. These are unique niches for which team PI has the expertise to develop and to address. Overall, the 5-year plan, which addresses very important questions for human health is well-defined.

Conclusion

During the last 5 years, the team PI has proven its excellent scientific quality by its achievements in term of (i) publications, (ii) capacity to get fundings, (iii) implication to research through education, and (iv) creation of a start-up company.

- **Strengths and opportunities:**

The particular strength of the team PI resides in its capacity to develop original research projects and to follow them up to the clinic. 11 clinicians are indeed members of the team PI and therefore have access to cohorts of patients. Last but not least, the team has a very original niche regarding the role of IL-33 secreted by endothelial cells in both asthma and sepsis.

- **Weaknesses and threats:**

The team has recently lost 3 technicians, and one is retiring next year. This low number of technicians could slow down the development of new concepts or approaches in this team. By its geographic location, the team remains isolated from the other immunology teams within the CIIL. A rapid relocation in buildings occupied by other CIIL teams will undoubtly help interactions, collaborations, and will impact on the quality of research.

- **Recommendations:**

The team should pursue the excellent ongoing work. The overall project is very interesting and carries a strong potential for important findings, with a special emphasis for the new project on endothelial IL-33.

The team has the skills and the tools and resources to be more competitive in terms of funding applications. The team leader should seek more connections with Pharmaceutical Industry.

While the overall quantity and quality of publications is very good, an effort should be made to increase the international scientific recognition by publishing in high-impact general journals. Some of the projects most certainly will yield results that may be published in such journals. In light of what it has seen in terms of preliminary data and expertise, the committee estimates that this team could be more ambitious.

Team 12: Transcriptomics and Applied Genomics (TAG)

Name of team leader: Mr David HOT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	2
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	4	4
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**	**7**

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

• Detailed assessments

Assessment of scientific quality and outputs

The team contributed 18 articles in peer-reviewed journals since 2008. Members of the team are co-authors in intermediate position on 17 of these articles, reflecting the shared platform activity of the team. Of note, 9 articles are co-authored with other teams of CIIL. Only one article was published on the scientific project of the team, with members of the team as first and last authors (small non coding RNAs in B. pertussis ; BMC Genomics, 2011). This modest output certainly reflects the time spent on academic research by this team (20%).

Assessment of the unit's academic reputation and appeal

The team actively collaborates with several teams of CIIL, and the development of new tools for transcriptomics and genomics, as well as pipelines for data analysis, were mentioned by several other teams. The team also collaborates with groups outside of CIIL, including abroad (Institute of Microbiology, Prague, Czech Republic, and Institute for Theoretical Chemistry, Vienna, Austria).

The team presented its results in three international meetings (Czech Republic, Netherlands, Ireland), and was invited to give a lecture in Prague (Czech Republic).

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

The team has many contracts with industry (e.g. Roquette Frères, Sanofi Pasteur). It created a joint venture unit called Pegase Biosciences to deal with the partnership between Pasteur Institute Lille and the company Gènes Diffusion. The team actively participated in the rapid characterization through whole genome sequencing of an outbreak of entero-haemorrhagic E. coli outburst in northern France during the summer of 2011, and got good media coverage for this achievement (including TV interviews).

Assessment of the unit's organization and life

The team TAG is composed of one University Professor (who will retire during the next five years), one senior scientist (the PI, CR at IPL), one assistant-professor, two engineers and one technician. Its organization is mainly centered on its technological platform activity, with only 20% of the efforts of the team dedicated to academic research.

Assessment of the unit's involvement in training through research

There are neither PhD students nor post-doctorants in the team. However, a PhD student with a CIFRE fellowship should be recruited shortly, for a bioinformatic project in collaboration with Gènes Diffusion. Training in the lab is limited to technicians (BTS) and Master students. The team organizes one thematic day for PhD students at the doctoral school Lille 1/Lille 2, on high throughput genomics. It is also in charge of a one week scientific course offered by Pasteur Institute of Lille on genomic tools, and of one Master teaching unit at the University Lille 1.

Assessment of the strategy and the five-year plan

The overall strategy is to continue to work as a technological platform in genomics, and as a research group in microbiology. The plan of the team is to (i) develop new applications for the Genomics facility (e.g. metagenomics, miRNA sequencing and analysis), and (ii) study the contribution of small non coding RNAs for the virulence of B. pertussis. The plan was judged very ambitious, especially in light of the limited resources available. The team will continue to split its time and personnel between two highly demanding tasks, at the risk of lowering its impact in both.

Conclusion

The team TAG is small and essentially dedicated to a technological platform activity in genomics. It is developing high-throughput technologies such as microarrays and next generation sequencing, which are highly valuable for the other teams of CIIL. This small team is also conducting independent research on virulence regulation in B. pertussis, although this represents only a small fraction of the outputs of the team as judged by the number of publications.

- **Strengths and opportunities:**

- the PI of the team is young and dynamic, and expressed with enthusiasm his ambition to lead an independent team within the CIIL;
- the team TAG has established a platform in genomics with a solid reputation, which benefits the other teams of the CIIL, and contributes to the visibility of the institute;
- the team has strong interactions with the economic environment;
- the team collaborates with a world leader on the virulence of B. pertussis.

- **Weaknesses and threats:**

- the team TAG has had a limited scientific production as an independent group in the past 5 years;
- the team is coming late in the field of next generation sequencing, which raises concerns about its capacity to be competitive;
- the team is coming late in the field of non-coding RNAs, a highly competitive field.

- **Recommendations:**

Regarding the activity as genomics technological facility, the current platform (one Ion Torrent PGM for which the team is a certified service provider) suits most of the current needs (metagenomics and bacterial genome sequencing) of the institute as demonstrated by the joint publications. It is up to the CIIL to decide how to support requests demanding higher throughput instrumentation (such as Illumina HiSeq), either by heavy investment in the team for instrumentation and personnel or by outsourcing to better established genomic cores or contract research organizations (CROs). Further developing Pegase Biosciences might be an opportunity. The committee also recommends to focus on specific applications in genomics and to improve services on data analyses. Emphasis should be placed on optimizing selected services in genomics rather than seeking to cover all applications in genomics. The bioinformatics group should be strengthened.

Regarding the research activity, the committee recommends to develop the projects (e.g. on non-coding RNAs) as part of collaboration with the team BRIPT. The nurturing of the research program within this internationally leading team will facilitate the recruitment of PhD students and grant application, thus preparing the transition towards the establishment of a new independent research team.

Team 13: Chemical Genomics of Intracellular Mycobacteria (CGIM)

Name of team leader: Ms Priscille BRODIN

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	5	3
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	**9**	**7**

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

• Detailed assessments

Assessment of scientific quality and outputs

The team was created only recently (October 2010) with a smooth and successful transition from Korean Pasteur Institute (IPK, Seoul) to the CILL. Most of the major outputs and publications for the five last years (17 in total) are of excellent quality (publications in Science, Nature Medicine, PLoS Pathogens (4), J. Medicinal Chemistry (3)), although one should note that the majority of the scientific production mentioned in the report dates from the period when IPK hosted the team leader. The team has been setting up visual high throughput screening of drugs, siRNA and mycobacterial mutants to search for new host and microbial targets to fight tuberculosis (TB).

Identifying host cell targets for antimycobacterial therapy is an expanding, promising but also very competitive field. The results generated since the team started at CIIL (e.g. role of CISH in host cell-mycobacteria interactions, role of LppM or PPE54 in mycobacterial virulence) should be published without delay. Very original and convincing data, currently under revision for publication in a high-ranked journal, were orally documented by the PI.

Assessment of the unit's academic reputation and appeal

The PI found a specific and fruitful niche in the field of high-content imaging systems for the study of host-pathogen interactions, and is clearly recognized as a pioneer in the field, as attested by several invitations to meetings and conferences, by the many collaborations she has with external and internal partners, and most importantly by the ERC starting grant she obtained.

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

The PI holds 4 patents, 3 being licensed, and has strong interactions with the private sector, which could be extended to non-profit organizations such as TB alliance or the Bill and Melinda Gates foundation.

Assessment of the unit's organization and life

The team encompasses, in addition to the PI, 6 postdoctoral fellows and 3 research assistants. Weekly meetings are organized.

Assessment of the unit's involvement in training through research

One PhD student has graduated during the evaluation period. One student is to be hired in the coming months, with secured funding from a Marie Curie ITN in which the PI is a partner member. 15 engineers were trained.

Assessment of the strategy and the five-year plan

The scientific objectives of the team CGIM are the identification and characterization of novel mechanisms involved in interaction between host cells and the pathogen M. tuberculosis. The strategy is based on the continued use of large scale, unbiased, screens, following either chemical mutagenesis or genome wide RNAi to trigger gene silencing. The project of the team CGIM is ambitious, and is based on both the exploitation of previous results (microbial and host cell targets), and on expanding the expertise and reputation of the team in the field of visual (4-D) high throughput screening. Only two post-doctoral fellows and 1,5 research assistants are working on target characterization, while the rest of the team is involved in screening activities; the balance between the screening activity and target characterization should be more equilibrated.

Conclusion

The various projects conducted, aimed at identifying and characterizing host cell targets for antimycobacterial therapy (e.g. dynamic 4D imaging *of M. tuberculosis* invasion, characterization of identified host restriction factors and bacterial effectors, high content screening, chemical biology and drug discovery) are ambitious and innovative. The PI succeeded in securing sufficient funding to develop these projects in the coming few years, including a prestigious ERC grant. Publications should appear in the coming months and few years.

- **Strengths and opportunities:**

The PI is clearly recognized as a pioneer in the field and succeeded in attracting a number of grants, including a prestigious ERC starting grant and others, postdoctoral fellows and research assistants. The contacts with industry are very good. The transition from IPK to CIIL has been achieved in a smooth and sucessful manner. The niche occupied by the team should be exploited and expanded. The focus on tackling of latent infections opens the field of HIV patients.

- **Weaknesses and threats:**

The support from the host institution regarding BSL3 animal facility issues is insufficient. The PI reported that heavy and constraining regulatory issues and lengthy procedures for animal importation clearly limits the extent to which the team can work with microbial pathogens and relevant animal models. This is not acceptable, and should be fixed promptly.

One or more permanent researchers should be hired, with at least one more HDR so that more PhD students can be supervised.

The occupied niche is very competitive and the PI should be more aggressive at publishing the team's results in high impact journals without delay.

- **Recommendations:**

The team, together with the CIIL management, must put pressure on the host institution to get support regarding the essential issues of BSL3 use and animal importation regulatory procedures.

The team should put more efforts in characterizing the hits and targets it identified (e.g. CISH and others). This will enable the group to publish quickly these data, and obtain recognition for this important work.

The team, including the postdoctoral fellows, should be more exposed to the scientific community through participation to international meetings and conferences.

Team 14: Biology and Diversity of Emerging Eukaryotic Pathogens (BDEEP)

Name of team leader: Mr Éric VISCOGLIOSI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	6	6
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)	3	3
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**13**	**12**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	7	
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	4	4

• Detailed assessments

Assessment of scientific quality and outputs

The research of the team is mainly focused on emerging eukaryotic parasites. One part of the team works on protozoa responsible for gastrointestinal infections like Blastocystis and *Cryptosporidium*, with great emphasis being given to their molecular epidemiology and phylogeny, comparative genomics and metagenomics, and development of animal models. The other part of the team works on the pathogenic fungus Pneumocystis.

Within these areas, the team has yielded, over the last 5 years, important contributions such as: (i) the genome sequence of a symptomatic isolate of a Blastocystis sp., and a hypothetical model of pathogenicity was proposed for this protozoan; (ii) the demonstration in the animal model that *Cryptosporidium* infection can induce digestive neoplasia. The scientific importance of these contributions is highlighted by the 113 articles published in peer-reviewed international journals during this period, of which 58 signed as main contributor. Over half of these publications appeared in journals with an impact factor above 3. The best ranked publication corresponds to the description of the Blastocystis genome sequence, which appeared in Genome Biology in 2011 (IF: 10.3) and in which the team leader is the unique co-author of the team, in 7th position. The dynamics of publication is good as at the time of file submission, the team had seven accepted articles for 2013 and one submitted. A significant proportion of the scientific production involves papers on Pneumocystis, and are authored by a scientist who will create a separate team for the next term.

Assessment of the unit's academic reputation and appeal

The strong national and international reputation of the members of this team is attested by the wide network of local, regional and international (Europe, North and South America, Asia, Oceania and the Middle East) collaborations. The team BDEEP is also involved as a coordinator or a partner in 12 national and international research projects. The attractiveness of the team is further illustrated by the training courses organized in laboratories, and by the hosting of several researchers, engineers, and technicians, from France or other countries. The team also trains on a regular basis post-doctoral fellows. Members of the team have evaluated research projects for French and foreign research agencies, and participated as chairman, “rapporteur” or examiner in about 30 PhD and HDR committees. The team leader was appointed as Guest Researcher at RIKEN (Japan) for two years (2010-11) and a PI as foreign member of the Royal Academy of Medicine of Cadiz (Spain).

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

Although this is a young team, it has already participated in several initiatives towards interaction with the socio-economic and cultural environment: (i) it is or was coordinator/partner in 9 national and international collaborative research projects funded by private companies, laboratories, associations and foundations; (ii) it co-coordinates the project ANR ALIA FISH PARASITES; (iii) it generated a specific training course for professionals of the fisheries sector; (iv) it is proposing its expertise to the company Newster; (v) the expertise of the team was requested for the ANR project ALIA PROTOFOOD.

Assessment of the unit's organization and life

The team BDEEP is composed of 10 members, currently composed of 1 full-time researcher, 1 University Professor, 5 Associate-Professors, 2 Hospital practitioners Associate-Professors, 1 Hospital practitioner, 1 Post-doc/Project manager, 2 Engineers, 1 technician and 4 PhD students. The research activities of the members are organized into two major themes: Blastocystis and Cryptosporidium. Besides, each member of the team is also involved in expertise activities with a scientific and /or economic interest. Some members were appointed for the hygiene and safety, scientific animation and communication. All researchers and students participate actively in seminars, conferences, and workshops within and outside the Centre.

Assessment of the unit's involvement in training through research

The team is hosting 33 students preparing theses in Pharmacy, Master 2 (11), Master 1 (6), Licence (12), and DU or BTS (19). Implication in formation through research is also attested by supervision of HDRs (2), post-doctoral fellows (4), PhD students (11), Medicine and Pharmacy theses and DES in Medical Biology (12). All PhD students have found employment, some of them abroad (2 in Japan and 1 in the USA). It should be noted that all PhD thesis defended so far (4) were finished on time (3 years).

The team has been collaborating with the Doctoral School Biology Health of Lille, and with Master 2 Research programs, teaching at the Faculties of Pharmacy and Medicine of Lille 2, School of Midwifery, IUT Biological Engineering of Lille 1, ISA Engineering School of Lille, Univ Catholique of Lille, and several foreign universities in Mexico, Venezuela and Lebanon. Some members of the team coordinate formations or diplomas and are members of committees at Faculties of Pharmacy and Medicine.

Assessment of the strategy and the five-year plan

The working plan of the unit for the next 5 years encompasses three major objectives : (i) determining the prevalence and biodiversity of Blastocystis in human populations ; (ii) tracking risk factors of transmission of Blastocystis and *Cryptosporidium* to humans ; and (iii) clarifying the pathogenicity of the different species and genotypes in order to identify factors associated with virulence.

To determine the prevalence and biodiversity of the parasite, the team will collect stool samples from 12 French hospitals and from a limited area in Lebanon that will include several hundred human samples. Genotyping of *Blastocystis* isolates will be performed by quantitative PCR targeting the SSU rRNA gene. Additional markers based on the mitochondrial or nuclear genomes of this parasite will also be developed. A large-scale epidemiological study performed in Lebanon will allow testing of hundreds of human and environmental samples for searching new reservoir and identify new modes of transmission of *Blastocystis* and *Cryptosporidium* in humans. Finally, relevant animal models will be developed to study the virulence of different strains/genotypes, and the interaction with host microbiota. Comparative genomics approaches will be used in these projects.

The study of virulence factors of Blastocystis is also an important step in the five-years plan of this team. The molecular characterization of the two single-copy SOD genes, both encoding dimeric FeSODs, present in the genome of Blastocystis, will be pursued. Both SODs of Blastocystis will be expressed in bacterial systems and purified to obtain crystals and X-ray structures (with the collaboration of ULB Bruxelles). Since parasitic protozoa only possess dimeric FeSODs slightly differing from the tetrameric MnSOD of human, the team intends to perform *in* silico design for the identification of inhibitors. DNA chips will be generated (with the collaboration of the Team TAG CIIL) and used for transcriptomic analyses of the parasite oxidative stress response. Functional genomics methods will also be developed (with the collaboration in particular of the Team MCBTG).

Globally, the strategy is not fully original, but covers classic protistology work that has to be done at this stage. The 5-year plan is promising, as it mixes field sampling of humans, animals and numerous environments, and the characterization of the isolates obtained by using high-throughput methodologies, to understand the relationship between the genetic characteristics of the strains and their phenotypes.

Conclusion

This is an internationally competitive group in the field of parasitology, with a very good productivity in terms of number of papers published in specialty journals. The team was working on both protozoa and fungi, but the project for the next five years will focus on infections by the protozoa Blastocystis and *Cryptosporidium*. The project is ambitious and should lead to novel insights on two emerging eukaryotic parasites.

- **Strengths and opportunities:**

The team has a long and strong experience in the field of protistology, and a strong capacity to be funded by academic or private environment. Due to limited competition in this field and high experience, the team has the potential to be one of the world leaders on this thematic. The team has good collaboration with national and European networks, allowing to obtain large collections of human samples. It also has the possibility to obtain numerous samples from areas where the parasite is supposed to be more prevalent than in France (e.g. Lebanon). The project appears very attractive with promising novel findings and insights.

- **Weaknesses and threats:**

- difficult field of research;
- strategy of publication that tends to favor quantity vs quality.

- **Recommendations:**

The team should complete the necessary classic protistology work rapidly, in order to move on to cell biology questions.This will increase the impact of the publications, as well as the international recognition.

In order to attain this goal, it will be necessary to secure funding for basic science projects on one of the parasites.

5 • Conduct of the visit

Visit dates:

Start: Wednesday, December 18th of 2013 at 1 pm

End: Friday, December 20th of 2013 at 5 pm

Visit site: Pasteur Institute, Lille

Conduct or program of the visit:

December 18th, 2013	
1.00 pm	Welcome (closed-door) visiting committee with the AERES Scientific Advisor
1.15 pm	AERES representative: the role and procedures of AERES
1.30 pm	Direction of the unit: Past and future; Discussion
2.20 pm	Team Molecular & Cellular Virology of Hepatitis C
	Talk (including past activities and projects) + discussion including time with the team leader
	Name of the team leader Mr Jean DUBUISSON
3.15 pm	Coffee break
3.30 pm	Team Lung Infection and Innate Immunity
	Talk (including past activities and projects) + discussion
	Name of the team leader Mr François TROTTEIN
4.20 pm	Team Pulmonary Immunity
	Talk (including past activities and projects) + discussion
	Name of the team leader Ms Anne TSICOPOULOS
5.10 pm	Team Nods-like receptors in infection and immunity
	Talk (including past activities and projects) discussion
	Name of the team leader Mr Mathias CHAMAILLARD
5.40 pm	Team Lactic Acid Bacteria and Mucosal Immunity
	Talk (including past activities and projects) + discussion
	Name of the team leader Mr Bruno POT
6.10 pm	Discussions with the team leaders
6.30 – 7.00 pm	Closed meeting

December 19th, 2013	
9.00 am	Team Plague and Yersinia pestis
	Talk (including past activities and projects) + discussion
	Name of the team leader Ms Florent SEBBANE

9.30 am	Team Bacterial Respiratory Infections, Pertussis and Tuberculosis (BRIPT)
	Talk (including past activities and projects) + discussion
	Name of the team leader Mr Camille LOCHT
10.20 am	Discussions with the team leaders
10.30 – 10.40 am	Closed meeting
10.40 am	Coffee break
11.00 am	Team Chemical Genomics of Intracellular Mycobacteria
	Talk (including past activities and projects) + discussion
	Name of the team leader Ms Priscille BRODIN
11.30 am	Team Cellular Microbiology and Physics of Infection
	Talk (including past activities and projects) + discussion
	Name of the team leader Mr Frank LAFONT
12.00 pm	Team Transcriptomics and Applied Genomics (TAG)
	Talk (including past activities and projects) + discussion
	Name of the team leader Mr David HOT
12.30 pm	Discussions with the team leaders
12.45 – 1.00 pm	Closed meeting
1.00 pm	Lunch
2.00 pm	Team Molecular and Cellular Biology of Toxoplasma Gondii
	Talk (including past activities and projects) + discussion
	Name of the team leader Mr Stanislas TOMAVO
2.30 pm	Team Biology and Diversity of Emerging Eukaryotic Pathogens
	Talk (including past activities and projects) discussion
	Name of the team leader Mr Éric VISCOGLIOSI
3.20 pm	Discussions with the team leaders
3.30 – 3.45 pm	Closed meeting
3.45 pm	Coffee break
4.00 pm	Team Molecular Signaling and the Control of Parasite Drowth and Differentiation
	Talk (including past activities and projects)+ discussion
	Name of the team leader MrJamal KHALIFE
4.50 pm	Team Basic and Clinical Immunology of Parasitic Diseases
	Talk (including past activities and projects) + discussion
	Name of the team leader Ms Sylviane PIED
5.20 pm	Discussions with the team leaders
5.30 – 5.40 pm	Closed meeting

December 20th, 2013

9.00 am	Parallel meetings with personnel:
	Discussions with engineers, technicians, administrative
	Discussions with staff scientists
	Discussions with students and post-docs

10.00 – 10.30 am	Discussion with the representatives of the managing bodies
10.30 am	Discussion with Doctoral school director
10.45 am	Discussion with the head of the Center
10.45 am – 5.00 pm	Private meeting of the visiting committee (in presence of the AERES scientific advisor) including lunch
5.00 pm	End of the visit

6 • Supervising bodies' general comments

Université Lille 2
Droit et Santé

Service de la Recherche, de la Valorisation
et de l'Information Scientifique (SeRVIS)
Affaire suivie par Christophe BOUTILLON
Directeur du SeRVIS
christophe.boutillon@univ-lille2.fr / 03.20.96.52.16

Le Président de l'Université

à

Monsieur le Professeur Pierre GLAUDES
Directeur de la Section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur (AERES)
20 rue Vivienne
75002 PARIS

Lille, le 8 avril 2014

V/Réf. : E2015-EV-0593560Z-S2PUR150007716-005709-RT

Objet : Observations de portée générale sur le rapport d'évaluation de l'unité *Centre d'Infection et Immunité de Lille*

Monsieur le Directeur,

Considérant le rapport que vous m'avez récemment transmis, je vous remercie au nom de l'Université Lille 2 et en particulier du directeur et des membres de l'unité *Centre d'Infection et Immunité de Lille,* pour la qualité de l'évaluation effectuée les 18, 19 et 20 décembre 2013 par votre comité d'experts.

Les appréciations et recommandations formulées seront soigneusement prises en considération et discutées avec le directeur de l'unité dans le cadre de la structuration de notre recherche pour le prochain plan quinquennal (2015-2019).

Vous trouverez ci-dessous les observations de portée générale sur le rapport d'évaluation de l'AERES, émises par le Directeur de l'unité *Centre d'Infection et Immunité de Lille.*

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma considération distinguée.

Pr. Xavier VANDENDRIESSCHE

Camille Locht
Directeur
Centre d'Infection et Immunité de Lille
Tel : 33-(0)3 20 87 11 51/57
Fax : 33-(0)3 20 87 11 58
Email: camille.locht@pasteur-lille.fr

Lille, April 7, 2014

To the members of the
Aeres Committee

Dear members of the Aeres committee,

Please consider the following comments made by the team leaders after reading the report prepared concerning the Center for Infection and Immunity of Lille (Inserm U1019, CNRS UMR8204):

- The CIIL members are pleased that the achievements of the CIIL after three years of existence made a very positive impression on the visiting committee and were judged remarkable.
- Concerning the weaknesses of the CIIL, the committee noted weaknesses in communication and decision making procedures. All strategic decisions are made by the executive council, composed of all the team leaders, and we wish to maintain this decision-making body. However, communication to the entire CIIL community about the decisions and other important issues needs improvement and will indeed be improved in the near future (e.g. more extensive use of the "conseil de laboratoire" will be made).
- The web-site was noted to be not operative enough. We agree with the visiting committee and have already started discussions at the level of the executive committee to improve the web-site. This will be a priority project for the next months.
- The visiting committee recommends to provide space and resources for new teams. This will indeed be possible, as new laboratory space will become available in a building, currently named CEREAT, on the campus of the Institut Pasteur de Lille. This building will be renamed by the Institute to be more consistent with the research activities of the CIIL.
- Concerning the genomics facility activity, the CIIL feels that this is an essential technological platform for almost all of the CIIL teams, as attested by the strong collaborations of this team with the other teams. This was recognized by the visiting committee, as it states that this team "actively collaborates with several teams of CIIL" and that its development of tools as well as its analysis solutions "were mentioned by several other teams", that this team "has established a platform in genomics with a solid reputation, which benefits the other teams of the CIIL, and contributes to the visibility of the institute". It should be emphasized that this platform has an IBiSA label and has acquired the HTS equipment via its partnership with Gènes Diffusion and the common program "Pegase Biosciences". It was in fact among the first laboratories in Europe to purchase this equipment.

- In accordance with the recommendations of the visiting committee we will strengthen the virology field in the CIIL. A first step into that direction is the new theme on Coronaviruses.
- Programs between teams in the CIIL will be further strengthened by fostering joined PhD projects (some already exist) and common grant applications (some also already exist, including a Horizon2020 application).
- The rules for access to and utilization of the BSL3 laboratory depend on the rules of the hosting institution, i.e. the Institut Pasteur de Lille. An agreement between the director of the CIIL and the next director of the Institut Pasteur de Lille has already been reached to work on the simplification of access and utilization rules.
- A common set of rules and procedures (for biosafety, hygiene and security) for all members of the CIIL is recommended by the visiting committee. Although we agree with the committee that this would be important, it will be difficult to implement, as CIIL personnel is employed by different institutions and hosted in buildings also owned by different institutions, each of them imposing their own rules. However, discussions with the different institutions will be engaged in order to reach this goal.
- The committee also recommends that funds should be made available to invite speakers not only in immunology, but also in virology, parasitology and bacteriology. We wish to respectfully bring to the attention of the committee that this is already the case, and the list of all events is regularly communicated to all personnel, including students, post-docs and technicians, of the CIIL.
- With specific respect to the MSCPGD team strategy regarding the "chemical screening" (by which we suppose is meant phenotypic screening using focused compound libraries), the team has a robust experience in the study of anti-schistosome (the SEtTReND FP7 project) and antimalarial drugs (Ferroquine with Sanofi Aventis, see recent related publications where the team was a main contributor). This background contributed to the team's success in obtaining funding for the A-ParaDDisE FP7 project, including the research on Schistosomiasis and Malaria. This latter project involves no less than 5 teams (including the SME Kancera) in phenotypic screening of compounds that will be supplied by 5 teams that carry out medicinal chemistry. The team will obviously be able to benefit from the help and support of these teams for any technical issues, as well as some teams within the CIIL. Phenotypic screening will form part of its future activities, but by no means the major part.
- Concerning the activities of team#10, we wish the committee to notice that field work is an important priority of the CIIL. Team #10 is aware of the threads related to its size and will set as its utmost priority the search for new senior scientists and post-doctoral fellows, as recommended by the committee. One important strategic aim for the next term will be a stronger integration of the field work with the other CIIL teams, such as those interested in infectious diseases of sub-Saharan countries and India (tuberculosis, malaria, schistosomiasis etc.). This may lead to a change in the title of the team and will be a major subject to be discussed with the scientific advisory board. The team feels that the clinical research platform EPLS and the LIA are important assets of the CIIL and provide a facility for CIIL members to access human samples and develop clinical studies/trials in African countries and India.

Team 1: Molecular and Cellular Biology of *Toxoplasma gondii* (S. Tomavo)

- Concerning the team's interaction with the social, economic and cultural environment, the team wishes to point out that the head and team members are also active in meetings: organization of kick off meeting of LabEx and symposia in France and abroad. The head and members are used to attend every two years the international congresses on Toxoplasmosis organized successively in New York, Corsica (as an organizer), Tübingen, Oxford and the head always acts as a chair of sessions. The head is also an invited speaker and chair at the XIII International congress on Parasitology (XIII ICOPA, Mexico City) on Protein Trafficking in Parasites (http://icopa2014.org/pdf/scientificProgram.pdf; August 10-16 2014). He is an invited speaker at the McGill University (Canada), University of Chicago (USA), Imperial College (England), University of Cambridge (England) and University of Dresden (Germany) during this assessment period. Editor or invited editor board of PLoS One, BMC Bioinformatics and invited editor of PLoS Pathogens. He is a Representative Officer (Chargé de Mission) of Cell Biology, Virus and Parasites, INSB, CNRS (2009-2013).
- Concerning the strategy and five-year plan, the team wishes the committee to note that *Toxoplasma gondii* is a great model to study protein trafficking. The simplification of the trafficking system makes it a model of choice that may help clarifying the role of already known or unknown proteins. For example, characterizing the function of TgSortilin has proven to reveal original data published in a high impact factor journal, and allowed to file a patent. Giving the requirement of TgSortilin activity for host cell invasion, this study is currently followed up by a very promising High-Throughput Screening (HTS) approach aiming at identifying chemical compounds inhibiting TgSortilin function and therefore parasite survival. As noted, the team also plans to explore the role of unknown candidate molecules that were identified through a Proteomic screen, thereby widening the area explored. Along the same line, the team plans to investigate promoters of rhoptry and microneme proteins in order to find new DNA motifs that could provide new insights into the regulation of the expression of these genes.
- Concerning the conclusions, the team cannot see "a period of significant weakness" during the course of the assessed period. The team has been evaluated AAAA+ (A+ for the project) in 2008 by the AERES. The last 5 years, it has published one Cell Host Microbe, PLoS Pathog, MCP, JBC, MM, JMB, 2 x PLoS One, with a total number of 15 papers for only 2 full-time researchers, including the head of team. In addition, the team raised 3.5 million euros as grants (LabEx, ANR, FEDER-Europe Community and Regional funds) the last two years.
- Concerning the weaknesses, the team is currently using alternative technologies to confirm the data obtained by inducible systems, in particular the conditional knock-out approach (LoxP and Cre-recombinase system). Furthermore, clear choices have been made regarding candidates to be studied in details: (i) AP1 and two of the most promising partners found by Co-IP and proteomics for the study of the anterograde transport and the exocytic activity; (ii) AP2 for the endocytic pathway; (iii) Vps35 and Vps26 for the retrograde transport; (iv) Biological functions of unknown and parasite-specific trafficking protein, and (v) Lipid transport during apical organelle biogenesis.
- Concerning the recommendations, the team presently has several international collaborations, which led to shared papers (Cell Host Microbe, PLoS Pathog, JBC, Mol

Microbiol): in the USA (one colleague in Chicago, others in New York) and the UK (Glasgow), and will do more if necessary.

Team 2: Molecular signalling and the control of parasite growth and differentiation (J. Khalife)

- Concerning the strategy and the five-year plan, first paragraph, last two sentences, the team wishes to point out that following the presentation of the project, a question was asked about the reverse genetics in *S. mansoni*. This was asked directly to R. Pierce, who answered this question by confirming that the only currently available technique, RNAi, is routinely used in the laboratory, with several published papers utilizing this methodology. Regarding this approach in *Plasmodium*, the team has published 3 papers, 2 in JBC and one in BMC Biology, signed as last author by the team leader. Therefore, it was not felt that "uncertainty about the background" was manifested in the response to this question.
- Concerning the weaknesses and the fact that the two schistosome leaders will retire within the next five years, the team is aware that it obviously requires the recruitment of a high-level senior researcher in order to continue this theme in Lille. The team is working hard to attract postdocs working or desiring to work on schistosomes with solid CVs to apply for permanent positions and is on the look-out for a more senior researcher, either already in the field or willing to join it. However, in case no permanent candidate on schistosomes is recruited and given the background of the researchers who will stay, the team will focus its projects on the biology of malaria. It should nevertheless be noted that neither R. Pierce (coordinator of the A-ParaDDisE project) nor C. Dissous, plan to retire in the immediate future. Both are involved in cutting-edge research in the field, publish regularly in the best journals in the domain and should be permitted to continue to do so.

Team 3: Plague and *Yersinia pestis* (F. Sebbane)

- Concerning the scientific quality and outputs, the team wishes to clarify that 17, and not 16 papers were published on Yersinia. Furthermore, since January, the team has a PLoS Pathogens accepted for publication, and a paper under minor revision in the Journal of Infectious Diseases. For both papers, all the persons associated to the work are only from the team. This brings the list up to 19 publications. The team would also like to underline that their contribution was not insignificant for 6 publications that were not signed as first or last author. Indeed,

1. M. Simonet is next to last author in the Vincent et al's paper (Emerg Infect Dis, 2008) because Vincent was associated in the Michel Simonet's former lab.
2. M. Simonet is next to last author in Dessein et al's paper (Gut 2009) because Dessein was Simonet's PhD student.
3. M. Simonet is next to last author in the Renaud et al's manuscript (J Clin Microbiol 2013) because he supervised the work with Gaillot. RJ Courcol associated to this work is also part of our team.
4. The team appreciates that the committee recognized that the PI (F. Sebbane) is next to last author in Vadyvaloo et al's paper (PLoS pathogens 2010) because of his real contribution, which is clearly stated in the manuscript.
5. The PI (F. Sebbane) is second author in the manuscript published in Emerg Infect Disease (Ayyadurai S, 2010)

6. The PI (F. Sebbane) and M. Simonet are second and next to last author, respectively, in the Vaccine paper published in 2010 (Daniel, 2010).

- Concerning the academic reputation and appeal, the emerging reputation of the team is attested by the fact that the PI has been invited in 2013 and is invited in 2014 to give lectures on plague for the Paris Institute Pasteur's Master 2, whereas there is a *Yersinia* team (headed by C. Carniel) working on plague at the Paris Institute Pasteur.
- Concerning the strategy and five-year plan, the committee considers that the projects are disconnected and that the team should prioritize some of them, notably because of the small size of the group. However, the team will be composed for the next 5 years of 2 full time researchers, 2 associated professors, 1 engineer and 3 technicians. The team does therefore not consider that the manpower is weak. Furthermore, the team will continue to hire PhD students and try to hire Post-Docs, and has collaborators. Lastly, it is true that each of the projects can stand on its own scientific merit but they are highly complementary to one another. For instance, project #1 (see below) could take advantage of the genes identified in the project #3. Genes identified in projects #1, 2 and 3 could ultimately be used in project #4. List of the 4 projects:
    1. Study the flea-borne transmission of plague
    2. Understanding the mechanism of plague in the mammalian host.
    3. Understanding the emergence of plague
    4. Developed an anti-plague vaccine.

The team agrees with the committee that it must put an effort on project #1, which is promising. However, the team cannot engage all the efforts here, because flea breeding is sometimes a real concern. For instance, the team already encountered flea reproduction problems. Sometimes for the flea breed for the overall colony is unhealthy. Furthermore, the team has recurrent bug contaminations of the flea colonies, meaning that it must restart the colonies. Lastly, flea infections are variable because the flea does not always bite like one would like. In other words, there is a risk to produce nothing if the team encounters a serious flea colony problem and increases variability in the infection that cannot be resolved quickly.
Project #2 is based on the PLoS Pathogens data and it happens that at the end ony very few genes are worthy of further study. Furthermore, the team has collaborators to understand the role of the genes of interest.
Project #3 is at high risk. However, it is the most promising, because it can open real new views on pathogenesis, evolution and ultimately lead to the production of numerous specific diagnostic tools for numerous diseases.
Project #4 is already under way. N. Lemaitre (associated professor) and her PhD student (M. Titecat) in collaboration with Locht's team already obtained the putative new vaccine of interest. Furthermore, animals have been vaccinated and will be challenged soon.
In conclusion, the team will mostly focus on project #1 and #3. However, the team must keep project #2 at background level, because it is a spare wheel in case of (i) project #3 (high risk) will provide no positive data and (ii) big trouble with the flea colony spoils project #1. Regarding project #4, it is already well advanced.
- Concerning the conclusion, the team appreciates that the committee recognized the difficulty to set up the laboratory and to run the laboratory on day-to-day basis due to the overwhelming national and local regulations. The team also appreciates that the committee pointed out these difficulties to explain the "modest production" in terms of publications. However, the team hopes that the information provided above will lead to the committee to consider that the production is

not so modest in the past years. Lastly, the team would like to mention that, in addition to the regulations, the production in terms of publications might not be considered very high in terms of numbers, because the team always tries to push the studies further to improve the impact of the publications (one committee's general recommendation for the CIIL). The publication in PLoS Pathogens (accepted recently) and in the Journal of Infectious diseases (1 published and one under minor revision) attest our claim.

Team 4: Bacterial respiratory infections, pertussis and tuberculosis (C. Locht)

- Concerning the interaction with the social, economic and cultural environment, the team wishes the committee to note that since the end of last year, 3 more patents have been licenced, and an important collaboration contract with industry has been obtained.
- Concerning the weaknesses and the recommendations, the team wishes to point out that meanwhile, important industrial funding for the further development of the pertussis vaccine has been obtained. Furthermore, the team has been selected for a Horizo2020 project on tuberculosis vaccine development (568,000 €) and two out of three ANR letter of intend have been selected.
- The team agrees with its weakness in terms of the number of PhD students. However, due to space constraints, it has decided to favour post-docs permanent researchers. Nevertheless, the team makes sure that at least one or two PhD theses will be defended per year (an PhD thesis output it has kept for over 20 years now).

Team 5: Cellular microbiology and physics of infection (F. Lafont)

- The team acknowledges the comments of the Committee on the "innovative technological approaches developed" and the "excellence" of the "production" and of the "international visibility". Also, the team acknowledges the other assets mentioned as "remarkable facets" on social economical impact and the achievements in training through research.
- The team recognizes that the strategy could have been more explained, as it does not deal with the study of one given pathogen and its related disease but rather to a basic question at the frontier of different fields, especially cellular microbiology and physics. This question is the following: How the mechanical properties of membranes engaged in the host-pathogen interactions modulate the immediate early signaling triggered at the plasma membrane discriminated from that activated during the internalization per se. It is more a cell biology question with pathogens used as tools. The signaling pathway selected is the autophagy and several pathogens, prototypes of different modes of entry, are studied in order to compare the molecular mechanisms involved. The team has chosen the risk of tackling a basic question, as this can lead to major discoveries that can thus be applied to a variety of "simple" questions (i.e. one application/pathogen-related disease).
- One aspect of the appraisal appears ambiguous to the team. On the one hand, the Committee recognizes the "important contributions on the role of autophagy in the control of intracellular bacterial infections" that are at the initiative of the team and not the result of collaboration. Moreover, the technological developments were made to solve a biological question raised when the team was established and based on the seminal work performed at the EPFL by the PI and for which the proofs of concept were documented during the presentation (i.e. the stiffness tomography that is not the result of any collaboration but developed within the team). On the other hand, the Committee states: "the strategy seems

to be mainly driven by collaborations". This contradiction should have been clarified. Whether by this statement the Committee did not mean scientific strategy but rather expressed some worries about the implication of the PI in Lille, as may be also reflected by the comments related to the priorities to be selected, sounds more likely. To answer this point, it will depend on the local resources the PI will obtain based on the recommendation of the AERES Committee.

Team 6: Molecular and cellular virology of hepatitis C (J. Dubuisson)

- The team thanks the AERES committee for its positive evaluation of its scientific activities, its academic reputation, its attractiveness to PhD students and post-docs and its organization and life. To answer some suggestions made by the committee, the team would like to add some details on three points raised in their report:
- The AERES committee mentions that the team could be more ambitious in its projects and develop broader screens. It is probably true that the team could have been more ambitious in the way the proposal was written. However, the team is currently developing more ambitious screens in collaboration with Team CGIM in the context of the HCV-ASSEMBLY project that has been selected in the Infect-ERA call of ERANET and for which the team is coordinator. In this project, the team will use high content confocal imaging with a genome wide small siRNA library to identify cellular factors involved in HCV assembly. In addition, complementary approaches will also be used by the Romanian and Danish collaborators. This was not included in the written document and it was just briefly mentioned during the visit of the committee because the team only received the notification of the selection a few days before the visit of the AERES committee. Furthermore, as mentioned below, the team also proposes to coordinate a more ambitious project by also using high-content screening with a genome wide small siRNA library to identify cellular factors involved in the life cycle of coronaviruses.
- In its recommendations, the AERES committee proposes that the team should establish active collaboration with the scientific community working in the field of MERS coronavirus research. The team agrees with them on this recommendation. However, at the time of visit of the evaluation committee, the MERS coronavirus project had only been initiated for a few months and it would have been difficult to already have established connections with other leaders in this field at that time. Meanwhile, the team has initiated a collaboration with another European group that is internationally recognized in the field. The team has also started some collaboration at the national level. In this context, the team has participated in a letter of intention for the ANR on a MERS coronavirus project in collaboration with other groups in France working on this virus. This letter of intention has been pre-selected and the team is currently finalizing the project that will be submitted. The team also proposes to coordinate a more ambitious project by using high-content screening with a genome wide small siRNA library to identify cellular factors involved in the life cycle of coronaviruses. The team has already the agreement of several French partners to collaborate on such a project and will try to secure funding for this coronavirus project by applying for an ANR grant.
- The AERES committee also recommends to make more effort to profit from patent exploitation and establish closer links with Industry in the area of HCV therapeutics. Actually, last year, the team contacted several big pharmaceutical companies with the objective to exploit its patents, but with the rapid development of potent anti-HCV

molecules arriving on the market, these big companies have stopped their investments in HCV antivirals. However, in the context of a novel anti-HCV molecule that the team is currently patenting, it has initiated some contact with an SME which is interested by the development of this molecule.

Team 7: Nods-like receptors in infection and immunity (M. Chamaillard)

- The team is delighted to learn that the evaluation committee thought that this is an excellent start for a young team with an outstanding academic reputation and appeal. Nonetheless, it was acknowledged that the team works in a very competitive field and has been very productive and successful in securing major funding and productive collaborations.
- The team would like to bring to the attention of the Aeres committee that it is a partner of two additional grants in addition to those mentioned in the committee's report. One is named Combinnate (ANR-13-BSV3-0014) and was previously referred within the written document, while the evaluation committee was informed about the second one at the site visit (ANR-13-PRTS-0006).
- Granting of these ANR grants seems to have raised some confusion within by the evaluation committee, as judged by the following sentence: "The strategy of the team does not seem entirely defined since the project presented during the site visit differed significantly from the one written in the document". For clarity, it is worth mentioning that the two additional fundings illustrate and legitimate the overall strategy of the principal investigator. Notably, it reinforces the proposed pathobiont discovery program by studying the pathogenesis of *Citrobacter rodentium* as a working model of enterohemorragic *E. coli* and clinical isolates of *Streptococcus agalactiae*. The team believes that the short period of time (only 10 minutes) did not allow for a more detailed presentation of the strategy written in the document and we would be grateful if the evaluation committee considers this comment on the very promising research strategy.
- The team also would appreciate if the committee considered that the team leader is an expert for foreign bodies (eg. Welcome trust, Broad Medical Research Program...)
- The team would also appreciate if the committee considered to which conferences team members were invited the principal investigator, like for other principal investigators within the CIIL. The principal investigator was indeed invited to several internationally established conferences (eg. Keystone symposium, College de France, Academie Nationale de Médecine, Fondation Biomérieux, European Immunology Group Meeting, International Congress of Mucosal Immunology, UEGW...) and/or international advanced schools (eg. Pasteur Immunology Course).

Team 8: Lung infection and innate immunity (F. Trottein)

- The team wishes to emphasize that since its creation in 2010 (fusion of three Inserm groups), it has been successful in developing a unifying theme of research while maintaining its policy of publication, securing financial support and recruiting new investigators (2CR, 1DR), a clear sign of attractiveness. Thanks (i) to the research program initiated in 2010, (ii) to novel and innovative projects developed by (new) scientist members and (iii) to higher intramural synergy, the next step will aim at enhancing the

impact factor of its scientific production. The team takes the comment of the committee as a strong encouragement for the future.

Team 10: Basic and clinical immunology of parasitic diseases (S. Pied)

- Concerning the weaknesses of the team, the team wishes the committee to consider that it results of a recent union of two research groups: "Malaria Immunopathophysiology" headed by Sylviane Pied from the Department of Immunology, Institut Pasteur Paris and "Clinical Parasite Immunology in Africa" headed by Gilles Riveau from Inserm U 547, Institut Pasteur de Lille. Therefore, during the first three years in the CIIL, it was firstly necessary to establish the adequacy and equilibrium between these two well-established groups. As noticed by the committee, the two groups have a strong involvement in research in the field in Africa and in India. A tremendous effort has been made by the team during the last 3 years to reinforce these links and this has been concluded by the creation of multidisciplinary consortia. The CRB-EPLS in Senegal (managed by Gille Riveau) is now an ISO 9001 platform for clinical trials and epidemiological research certified by Inserm and WHO. The CRB-EPLS staff consists of 30 employees (CDI and CDD). The "Laboratoire International Associé" CNRS-DBT SIGID (managed by Sylviane Pied) is an operational network of two UMR CNRS in France and four Research Institutes associated with two clinical platforms located in 3 regional states in India. EPLS and the LIA SIGID allow the feasibility and the direct integration of the clinical and basic research programs of the team. These activities have not been taken into consideration by the committee and there is no mention of its efforts on translational research and valorization. However, the strategy deployed and efforts to facilitate close collaboration between the two teams support reconciliation to give a greater cohesion.
- Concerning the publication record, despite the small size of the team it published 34 articles. Since December 2013, 3 articles were published, 4 are in press, 2 are under revision and 8 in preparation. Therefore, the team feels that its publication records is comparable to other well-evaluated French teams (see the list of the recent publications below).
- Concerning the recommendations, the team acknowledges that the committee finds that expertise in parasite immunopathophysiology, both in human and experimental models is well-recognized and that the technical feasibility of the proposed projects is very good when taken individually. We acknowledge also the fact that a recommendation has been made to "increase our size to provide full support to the ongoing projects by recruiting additional permanent researchers" and that this will be taken into account in the recruitment strategy of researchers in the CIIL.

Team 12: Transcriptomics and applied genomics (D. Hot)

- Concerning the remarks on the continuation of the research activity alongside the activity as a genomics facility, the team would like to stress that the development of its research activity was supported and encouraged by the previous AERES committee evaluation in March 2009 (EVAL-0593560Z). The team agrees on the fact that more collaboration with the BRIPT team could strengthen the development of its own research projects, although quite strong interactions already exist between the 2 teams (sharing of skills, discussions,

common lab-meetings, co-publications ...). Since the visit of the committee, two additional publications were accepted (one in BMC Genomics and one in Pathogens), with members of the team as first and last authors, pointing to its bioinformatics investment. This investment still needs to be strengthened as written in the report, starting by stabilizing the research engineer in bioinformatics, presently in a non-permanent position ending in December 2014.

- Concerning the genomics facility activity, the team does not fully understand the discrepancy between the rather positive remarks at different parts of the assessment and the conclusion remark in the 'recommendations' final part. Indeed, one can read first that the team "actively collaborates with several teams of CIIL" and that its development of tools as well as its analysis solutions "were mentioned by several other teams", that it has "many contracts with industry", that the team "has established a platform in genomics with a solid reputation, which benefits the other teams of the CIIL, and contributes to the visibility of the institute" and "has strong interactions with the economic environment". The team feels that these remarks are inconsistent with the recommendation that the CIIL has "to decide how to support requests demanding higher throughput instrumentation (such as Illumina HiSeq), either by heavy investment in the team for instrumentation and personnel or by outsourcing to better established genomic cores or contract research organisations" (this remark echoes back the recommendation in the part 'Assessment of the unit' which says "whether the genomic platform should be kept internal or externalized has to be considered ..."). The team did not ask for new equipment, such as an Illumina HiSeq because, as stated during the presentation, this piece of equipment is already available on the IPL campus (in UMR8199), is shared in the team's "LIGAN" network labelled IBiSA and has already been used for several projects. The team wishes to emphasize that the HTS equipment was fully supported by the partnership with Gènes Diffusion and the common program "Pegase Biosciences". The team would like also to point out that it was among the first laboratories in Europe to purchase this equipment. Secondly and more importantly, the team does not understand why the CIIL should think of outsourcing its activities to 'better established genomic cores' considering the satisfaction of the colleagues from other CIIL teams (as noticed by the committee itself).

Team 13: Chemical genomics of intracellular mycobacteria (P. Brodin)

- The team is sorry to read that the committee felt that most of the team was doing HCS projects. Actually all 5 post-doctoral fellows are working on characterizing bacterial and cellular pathways used by the mycobacterium for its intracellular colonization and on chemical biology approaches, stemming from the data gathered from the screens done in IP Korea. The three research assistants are involved in the routine experiments such as drug testing on the *M. tuberculosis* infected macrophages or *in vivo* efficacy in mice. Only the visiting post-doc Maria Fernanda, who was paid by the Fiocruz to learn the HCS technique, did spend time on a siRNA screen set-up.
- Concerning the recommendations, the team realizes that the submitted report did not contain the list of conferences during which the various current team members gave presentations (selected communications or poster), which is now given below. We would like to emphasize of the facts that all the team members currently in the laboratory have only joined the team less than 3 years ago and that each of them has already participated in

either EMBO Conferences or Gordon Conferences (participation in conferences are provided below).

- Finally, the team wishes to bring to the attention of the committee that a paper of the team has recently been accepted for publication in Cell: Marion E, Song OR, Christophe T, Babonneau J, Fenistein D, Eyer J, Letournel F, Henrion D, Clere N, Paille V, Guérineau N, Saint André JP, Gersbach P, Altmann KH, Stinear T, Comoglio Y, Sandoz G, Preisser L, Delneste Y, Yeramian E, Marsollier L, Brodin P. 2014. Mycobacterial Toxin Induces Analgesia in Buruli Ulcer by Targeting the Angiotensin Pathways. Cell, accepted for publication.

Team 14: Biology and diversity of emerging eukaryotic pathogens (E. Viscogliosi)

- In its global report, the committee suggests focusing the research activities of the team on a single model, *Blastocystis* or *Cryptosporidium*. However, the team wishes to remind that its major results achieved in recent years on the molecular epidemiology, transmission and pathogenicity of *Blastocystis* and *Cryptosporidium* are promising, and therefore, the team wishes to pursue this. Consistent with this wish, the experts pointed out that the proposed project focusing on infections by these two parasites is "ambitious", "very attractive", and "should lead to novel insights". Moreover, the continuation of this project is consistent with the number of staff involved. In addition and as also detailed below, this project is in part already funded through different research contracts. For these reasons, the team wishes to maintain and develop its research activities on these two parasites for which they have proven knowledge at an international level.
- The committee underlines the "lack of visibility on the financial viability of BDEEP after the separation from the mycology group". The team believes that this statement is based on an incorrect analysis of the various fundings of the team. Indeed, 7 of the 9 fundings obtained from industrial and private companies in the last five years involved members of the team as coordinator or partner (E. Viscogliosi, L. Delhaes, G. Certad). This is also the case for 7 of the 12 academic fundings previously obtained by the team. On the other hand, many of these contracts are currently funding the proposed project which will add the annual financial support of CIIL. In addition, several applications for funding regarding the *Blastocystis* / *Cryptosporidium* / microbiota project have been made in response to different calls (Program Epigénétique et Cancer, Plan Cancer, ITMO 2014; Fondation pour la Recherche Médicale, Analyse bioinformatique pour la recherche en biologie 2014; Project IMAGin-CF, Vertex Grant – full proposal under reviewing; Fédération hospitalo-universitaire FHU 2014; InfectERA-2014; RIIP ACIP 2014; Programs Hubert Curien 2015 Cédre France - Liban and Utique France - Tunisie, Fondation Biomérieux 2014...). As stated by the experts, the team has "a strong capacity to be funded by academic or private environment" and is consequently confident in obtaining additional fundings.
- The committee indicates that the strategy of publication of BDEEP "tends to favor quantity vs quality" even if it also highlights in its report "a very good productivity in terms of number of papers published in specialty journals". At the date of submission of our report, the team had published 121 articles and the majority (105) in peer-reviewed international journals. Over half of them (55) had an impact factor between 3 and 10 in leading journals in environmental and medical microbiology, parasitology, genomics and evolution. The average IF of the articles range between 3 and 4, which emphasized the quality of the team's production in its disciplines. This production was complemented by the publication

of 14 book chapters. This being recalled, one of the team's objectives will obviously be to increase the impact of its publications over the next 5 years. This has promptly been initiated in the weeks following the evaluation by the publication of articles in journals of IF>3, such as BMC Infect Dis, BMC Microbiol and J Clin Virol, IF>5, such as Dis Model Mech (in press), IF>10, such as Am J Resp Crit Care Med (in press) and the submitting of another article to Emerg Infect Dis (IF>5). The valorisation of our studies in term of publications will be pursued and strengthened.

Finally, in the name of all the members of the CIIL, I wish to thank the evaluation committee for the time and effort they took in analysing the activities of the CIIL, and for the valuable recommendations that will certainly help us to further improve the quality of the work done in our center.

Sincerely yours,

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Le Président de l'Université

Pr Xavier VANDENDRIESSCHE

Université Lille 2
Droit et Santé

Participation in national/international conferences by team #13 (headed by P. Brodin)

2013

13/01 Host-pathogen interactions, iRTSV, Grenoble, France, 2013/06/06

P. Brodin, Phenotypic visual screenings on the [M. tuberculosis-host macrophage],

13/02 Glaxosmithkline, Tres Cantos, Espagne, 2013/01/09

P. Brodin, Identification of Molecular Determinants of M. tuberculosis Colonization into Host Cells by High Content Cell-based Screening,

13/03 Mycoclub 3, Toulouse, 2013/05/21

R. Veyron-Churlet, Role of the mycobacterial lipoproteins, LppM and LppN, in the intra-macrophagic fate of Mycobacterium tuberculosis,

13/04 Mycoclub 3, Toulouse, 2013/05/21

C. Queval, Cytokine-inducible SH2-containing protein (CISH) is involved in Mycobacterium tuberculosis intracellular survival in macrophages, Poster

13/05 CIIL 2013 International symposium, Lille: Revisiting Paradigms in Innate Immunity, 2013/10/08

C. Queval, The host factor CISH controls innate immunity to promote Mycobacterium tuberculosis intracellular survival in macrophages.

13/06 EMBO meeting 2013, EMBO|EMBL Symposium: New Approaches and Concepts in Microbiology, EMBL Heidelberg, Germany, 2013/10

O.R. Song, Discovery of novel host restriction factors controlling Mycobacterium tuberculosis invasion into pneumocytes, Poster

13/07 EMBO meeting 2013, EMBO|EMBL Symposium: New Approaches and Concepts in Microbiology, EMBL Heidelberg, Germany, 2013/10

R. Iantomasi, Tracking the fluorescent Mycobacterium bacilli into fluorescent macrophages by automated confocal imaging, Poster

13/08 Gordon Research Conference on Tuberculosis Drug Development, Barga, Italy, 2013/07

V. Delorme, An *in vitro* granuloma model for the high-content screening of drug/nanoparticle formulations, Poster

13/09 Congrès du GERLI, St-Jean Cap Ferrat, 2013/11

V. Delorme, De Mycobacterium tuberculosis à la protéomique chimique: application et greffage d'inhibiteurs de lipases et de carboxylesterases.

2012

12/01 Second Sino-French Symposium on Transdisciplinary Infectious Diseases Wuhan, Chine, 2012/10/31

P. Brodin, Discovery of novel host factors, M. tuberculosis effectors and Small molecule antimycobacterial compounds using High Content Screening,

12/02 DIMmalinf Ile de France, Réunion annuelle, Paris, France, 2012/10/17

P. Brodin, High Content Screening in Infectious Diseases: Application to M. tuberculosis,

12/03 Netherlands Kanker Institute, Amsterdam, Pays Bas, 2012/10/15

P. Brodin, Interrogation of chemical, bacterial mutants and siRNA libraries for the identification of molecular determinants of M. tuberculosis colonization into host cells,

12/04 RSTMH, Biennial meeting 2012, Warwick, Angleterre, 2012/09/19

P. Brodin, Fishing novel host factors, M. tuberculosis effectors and Small molecule antimycobacterial compounds using High Content Screening,

12/05 EMBO Conference Tuberculosis 2012, Paris, France, 2012/09/14

P. Brodin, High Content Cell-based Screening Insight in biology and drugs targets of M. tuberculosis,

12/06 Keystones Symposia Global Health Series, Kampala, Uganda, 2012/05/16

P. Brodin, High-content screening of M. tuberculosis –Infected macrophage as a pre-clinical model for the development of Novel Anti-tuberculosis Drug candidates,

12/07 Ecole Polytechnique de Lausanne, Suisse, 2012/05/09

P. Brodin, HCS and Intracellular Mycobacteria,

12/08 EMBO Conference on Subversion of Host Cellular Organization and Functions by Pathogens, Villars-sur-ollon, Suisse, 2012/05/07

P. Brodin, High-Throughput High Content Screen on the M. tuberculosis –Infected macrophage,

12/09 Institut du Thorax, Nantes, 2012/03/01

P. Brodin, High Content Screens on Intracellular Mycobacteria,

12/10 EMBO Conference on Subversion of Host Cellular Organization and Functions by Pathogens, Villars-sur-ollon, Suisse,

C. Queval, CISH is a host cofactor involved in intracellular Mycobacterium tuberculosis replication in macrophages, Poster

12/10 EMBO Conference on Subversion of Host Cellular Organization and Functions by Pathogens, Villars-sur-ollon, Suisse,

O.R. Song, GTPase-activating protein of ADR-ribosylation factor 1 (ARFGAP1) restricts Mycobacterium tuberculosis internalization into pneumocyte type II A549 cells, Poster

12/11 EMBO Conference on Subversion of Host Cellular Organization and Functions by Pathogens, Villars-sur-ollon, Suisse,

R. Iantomasi, Can Mycobacterium tuberculosis induce apoptosis or necrosis? Insight from Mycobacterium tuberculosis infected macrophage phenotypic assays using automated confocal microscopy, Poster

2011

11/01 Mycoclub 2, Tours, 2011/09/26

P. Brodin, Chemical and Genetic Phenotypic Screens on M. tuberculosis –colonized macrophages,

11/02 Institut Pasteur, Paris, 2011/09/15

P. Brodin, Intracellular Persistence of M. tuberculosis - novel insights from cell-based high content screening,

11/03 Institut de Recherche Interdisciplinaire, Villeneuve d'ascq, 2011/06/16

P. Brodin, Criblages chimiques et génétiques par microscopie confocale automatisée d'inhibiteurs de la croissance intracellulaire de M. tuberculosis,

11/04 Keystones Symposia on Tuberculosis, Vancouver, Canada, 2011/01/15

O.R. Song, Host Survival Factors involved in Mycbacterium tuberculosis Intracellular Growth, Poster

11/05 Mycoclub 2, Tours, 2011/09/26

O.R. Song, ARFGAP1 is a host defense factor which regulates Mycobacterium tuberculosis survivals in A549 cells, Poster,

Recent publications by team #10 (headed by S. Pied)

- Gaayeb L. , El Safadi D., Meloni D., Cian A., Poirier P., Wawrzyniak I., Delbac F., Dabboussi F., Delhaes L., Seck M., Hamze M., Riveau G., and Viscogliosi E. Children of Senegal River Basin show the highest prevalence of Blastocystis sp. Ever observed worldwide. *BMC Infectious Diseases* 2014, 14:164-173.

- Gaayeb L., Sarr J.B., Cames C., Pincon C., Hanon J-B., Ndiath M.O., Seck M., Herbert F., Sagna A.B., Schacht A-M., Remoue F., Riveau G., and Hermann E. Effects of Malnutrition on Children's Immunity to Bacterial Antigens in Northern Senegal. *Am. J. Trop. Med. Hyg.*, 2014, 90 : 566–573.

- Pied S., Trying the Triangle. *International Innovation*, 2014i, 129: 83-85.

- Gaayeb L.; Pincon C., Cames C., Sarr J.B., Seck, M., Schacht A-M., Remoue F., Hermann E., Riveau G. Immune response to Bordetella pertussis is associated with season and undernutrition in Senegalese children. *Vaccine*. In press.

- Sengupta A., Ghosh S., Das B. K, Panda A., Tripathy R., Pied S., Ravindran B., Pathak S, Sharma S, singh H, Sonawat M., Host Metabolic Responses to Plasmodium falciparum infections in Eastern India evaluated by ^{1}H NMR. (*Metabolomics*. In press).

- Guiyedi V. , Bécavin C., Herbert F., Gray J., Cazenave P.-A., Kombila M., Crisanti A., Fesel C, Pied S. Asymptomatic Plasmodium falciparum infection in children correlates with high plasmatic levels IL-10 associated to antibody to Merozoite Surface Protein 3 and autoantibody production (CID, In press).

- Blanc A.-L., Gorgette O., Bandeira A., Malissen B., Cazenave P.-A., Pied S. Naturally occurring CD4+CD25+Foxp3+ regulatory T cells aggravate experimental cerebral malaria by suppressing the CD4+ effector response (*PlosOne*, In press).

- Shrivastava SK., Delcroix-Genete D., Truccolo J., Chêne A, Soulard V., Cazenave P.-A., Roland J., Herbert F., Das B., Vigário AM, Pied S. Imaging and genes profiling of astrocytes and microglia upon interaction with malaria parasite: role in cerebral malaria. (*Plos Pathogens*, In revision).

- Riveau G., Dompnier J-P., Schacht A-M., Charreau I., Seck M., Waucquier N., Libersa C., Alboulker J-P., Gaayeb L., Schaus C., Mc Namara M., Senghor S., Saïdi Y., Boutouaba S., Béchu P., Capitan C., Gelé P., Capron M., Sebastiani C., Levy-Marchal C., Biomedical Research Center EPLS, and Capron A. Safety, immunogenicity and efficacy of rSh28GST as a vaccine against urinary schistosomiasis: A randomized double-blinded Clinical Trial in Senegalese children (In revision *PloS Med*).

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