Research evaluation

EVALUATION REPORT OF THE UNIT

M3I - Modèles Insectes d'Immunité Innée

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Strasbourg

Institut national de la santé et de la recherche médicale - INSERM

Centre national de la recherche scientifique - CNRS

EVALUATION CAMPAIGN 2022-2023
GROUP C

Report published on July, 11 2023

High Council for evaluation of research and higher education

In the name of the expert committee[1] :

Matteo Iannacone, Chairman of the committee

For the Hcéres[2] :

Thierry Coulhon, President

Under the decree n° 2021-1536 of 29th November 2021:

[1] The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

[2] The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson:	Mr Matteo Iannacone, San Raffaele Scientific Institute & University, Italy
Experts :	Ms Núria Busquets, Institute of Agrifood Research and Technology, Spain Mr Jean-Christophe Deschemin, Inserm, Paris (supporting personnel) Mr Mohamed-Ali Hakimi, Inserm, La Tronche (representative of Inserm CSS) Mr Pierre Peyret, Université Clermont-Auvergne (representative of CNU) Mr Harald Wodrich, Université de Bordeaux (representative of CoNRS)

HCÉRES REPRESENTATIVE

Mr Jacques Dutrieux

CHARACTERISATION OF THE UNIT

- Name: Modèles Insectes d'Immunité Innée
- Acronym: M3i
- Label and number: UPR9022
- Composition of the executive team: Mr Jean-Luc Imler

SCIENTIFIC PANELS OF THE UNIT

SVE4 Immunité, infection et immunothérapie

THEMES OF THE UNIT

The unit is single team but organized in 7 research groups of 5-12 people. These groups develop projects focusing on four scientific themes:
-antiviral immunity, from detection of infections to effector mechanisms;
-antiparasitic immunity, from genetics to the control of disease transmission;
-characterization of the effector mechanisms regulated by the Toll and IMD pathways of innate immunity;
-host defence against intestinal infections.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The research unit UPR9022 (Unité Propre de Recherche) "Immune Response and Developments in Insects" was created in 1992 and became one of the three CNRS units hosted at the Institut de Biologie Moléculaire et Cellulaire (IBMC). The laboratory, created by Jules Hoffmann, was previously a team associated with CNRS, under the names Humoral Biology of Insects (1969-1984) and Endocrinology and Immunology of Insects (1984-1991), and was in the Institute of Zoology from the University of Strasbourg at a short distance from IBMC on the central campus. Jean-Marc Reichhart succeeded to Jules Hoffmann and directed the unit from 2007 to 2017. Since 2002, the unit hosts a group working on mosquito immunity. Initiated by Elena Levahina, now director of the Vector Biology department at the Max Plank Institute for Infection Biology in Berlin, the team is now directed by Stéphanie Blandin and is supported by Inserm (ERL Inserm U1257). Jean-Luc Imler, who was deputy director of the unit from 2013 to 2017, became director in 2018 and the unit was renamed "Insect models of innate immunity".

RESEARCH ENVIRONMENT OF THE UNIT

The unit M3i is part of the Research federation FR1589 (IBMC)(https://ibmc.cnrs.fr/en/). IBMC hosts two other research units, ARN (Architecture and reactivity of RNA, UPR9002) and I2CT (immunology, immunopathology and therapeutic chemistry, UPR3572). The director of M3i was also the director of the FR1589 for the period of evaluation. A common theme of interest for the three research units of IBMC is the understanding of the molecular and cellular biology of infections in a broad sense, from single cell or single molecule analysis to the pathophysiology of immune disorders. The new insectarium and its BSL2 and BSL3 laboratories, constructed and equipped during the last period under the impulse of M3i, open new opportunities for collaborations between the three units. The document 1 in the portfolio presents the insectarium.

Four groups of M3i are affiliated to the Labex NetRNA, which focuses on the biology of regulatory RNAs (https://labex-netrna.cnrs.fr/). This Labex was renewed for the period 2021-2028 with a total budget of 8M€ and is now part of the Interdisciplinary Thematic Institute IMCBio (Integrative Molecular and Cellular Biology), which includes the graduate school IMCBio and three other Labex (INRT, Mitocross, HepSYS). One researcher of the unit M3I is deputy director of the IMCBio graduate school. In addition, the team ERL Inserm U1257 is affiliated to the Labex Parafrap.

The new insectarium building was fully equipped with the Equipex I2MC (Insectarium for molecular and cellular infectiology; 3.2M€, 2012-2022). This funding allowed to equip a transient insectary facility in the nearby Physiology Institute, which was used between 2016 and 2018 during the construction of the new building, and then to equip mouse and insect facilities of the insectarium. The Equipex was also instrumental to hire a young and dynamic engineer, who followed the construction of the building, participating in all meetings with the architects and the contractors, and who supervised the acquisition of the equipment, some of which had to be tailor made (e.g., the glove boxes to handle the infected mosquitoes in the BSL3 facility). After three years on temporary contract, CNRS opened a permanent position to hire this engineer, who is now affiliated with the FR1589.

UNIT WORKFORCE: in physical persons at 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	3
Lecturer and associate lecturer	2
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	4
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	15
Subtotal permanent personnel in active employment	**25**
Non-permanent teacher-researchers, researchers and associates	7
Non-permanent research supporting personnel (PAR)	5
Post-docs	5
PhD Students	16
Subtotal non-permanent personnel	33
Total	**58**

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING "OTHERS".

Employer	EC	C	PAR
CNRS	0	2	10
Université de Strasbourg	5	0	3
Inserm	0	3	2
Total	**5**	**5**	**15**

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	1 215
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	2 379
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	3 990
Own resources obtained from international call for projects (total over 6 years of sums obtained)	1 035
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	3 128
Total in euros (k€)	11 747

GLOBAL ASSESSMENT

The unit's scientific interests have been firmly focused on immune response and development in insects. Although the unit is a single team, it is organized in 7 research groups focused on 4 scientific themes: 1) antiviral immunity, from detection of infections to effector mechanisms; 2) antiparasitic immunity, from genetics to the control of disease transmission; 3) characterization of the effector mechanisms regulated by the Toll and IMD pathways of innate immunity; and 4) host defence against intestinal infections. Amongst the major contributions to the field in the reporting period, we highlight: the finding of a novel evolutionary conserved resilience mechanism in enterocytes; the impact of the RNAi pathway on dengue and Zika virus dissemination in the insect host; the role of proteases in activating innate immunity as well as highly innovative topics such as the recognition of cancer cells in drosophila or the characterization of novel pattern recognition receptors in drosophila.

The scientific production of the unit is excellent with 57 articles and 18 reviews published in very prestigious multidisciplinary journals (*Nature, Nature microbiology, PNAS, Cell Host & Microbes, Mol. Cell, Immunity, Cell reports*...). Two thirds of these publications are signed as first, last or corresponding author by members of the unit. Although the quality of the scientific production is high, the unit's output in terms of quantity of published papers is relatively modest considering the unit's size. The scientific visibility is also excellent with the participation in 48 national and 126 international congresses and seminars. The unit is attractive for the recruitment of doctoral students (35) and post-doctoral students (12) at the international level because of its expertise and reputation but also because of the availability of funding. Four members of the unit have been distinguished by national and international prizes. The researchers of the unit are also members of scientific academies and recognized institutions (US national academy of Sciences, Académie française des sciences, EMBO, Institut Universitaire de France).

One particular strength of the unit has been the creation of a state-of-the-art insectarium with BSL2 and BSL3 areas that enables exciting new research into vectors and agents of human disease (e.g., mosquito-transmitted dengue virus). The technical resources are crucial but insufficient for the expected developments, notably inside the insectarium. The unit received substantial funding from several agencies during the reporting period, some of which extends beyond 2022. The unit has diversified its funding sources by participating in competitive calls at the national, European, and international levels. One notable funding is Equipex (€3.2 million, 2012-2022), which provides the necessary funds for the construction of the Insectarium, but also for its operating costs. By contrast, there are no ERC grantees among the team leaders during this period.

The unit attracts national and international young research fellows, offering a supportive environment for their professional development either in the academia or in the industry.

While the scientific and societal impact of the research is remarkable, the major weaknesses remain the limited translational research, therapeutic and industrial applications.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The previous review committee recommended securing adequate funding to support key technical staff for the insectarium. Despite management's best efforts, this issue appears to be unresolved because the CNRS, the primary body institution, only offers short-term contracts (CDD type) and has not created any permanent positions. While the University Unistra provided a replacement for an engineer who left due to health reasons in 2016 and Inserm created a technician position, it appears that this is insufficient to strengthen the insectarium's existing technical staff.

The committee also recommended that the most important results be prioritized and published as soon as possible, a strategy that ensures that all doctoral students are published as first or co-first authors at the end of their thesis or at least a few months after the defense. Using the Hcéres documents, we cannot verify that all students also sign an article as first author. They were listed as authors in 57 articles/82, with no indication of rank. It is difficult to say whether or not this recommendation was followed by action, since the group leaders reacted negatively to this request and maintained their policy of "giving priority to the quality of publications over their number."

B - EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the unit's resources

The unit has very good human and financial resources to carry out its scientific projects with an adequate supervisory staff. The infrastructures are well adapted to the size of the unit and provide a remarkable technological offer, including an BSL3 insectarium. There is opportunity for improvement in the hiring of more tenured technical staffs.

Assessment on the scientific objectives of the unit

It is an outstanding unit of the highest international standard, making significant scientific discoveries with far-reaching implications. The research focus has been significantly expanded in recent years to enable novel, breakthrough discoveries in new areas. The overall feasibility of the five-year plan is very good.

Assessment on the functioning of the unit

The Institute's management is excellent.

1/ The unit has resources that are suited to its activity profile and research environment.

Strengths and possibilities linked to the context

The M3i unit has permanent scientists from CNRS (n=2), Unistra (n=5), and Inserm (n=3). The unit is attractive and has enabled the hiring of a tenured researcher at CNRS and the promotion of two faculty members to professor. Regarding technical support, engineers or technicians from CNRS (n=6), Unistra (n=3), and Inserm (n=1) complement the staff, which totaled 20 people during this period. The unit hosted 23 non-permanent staff (12 PhD students, 7 post-docs, 4 technical staff) during this period, reflecting its attractiveness. There is a good mentor-mentee ratio, reinforced by 4 HDRs (French diplomas entitling to supervise PhD students) during the reporting period, allowing to host a large number of PhD students in the unit: 33 during the reporting period.

The unit received substantial funding from several agencies during the reporting period, some of which extends beyond 2022. The unit has diversified its funding sources by participating in competitive calls at the national, European, and international levels. One notable funding is Equipex (€3.2 million, 2012-2022), which, under the direct supervision of the Director, provides the necessary funds for the construction of the Insectarium, but also for its operating costs. In contrast to the strong participation of M3i teams in the PIA calls (Labex, Equipex, Idex, Eur, etc.), there are no ERC grantees among the team leaders during this period. It is worth mentioning the ERC starting grant awarded to a group leader for the period 2011-2016. However, given the date on which this five-year grant was awarded (2011), it is more appropriate to consider this grant in the context of the previous period.

All financial resources are shared, in a collective spirit but also of optimization of resources given the size of the unit. It is worth noting that all permanent staff were invited to apply for funding during this period and had a high success rate.

The unit has been a pioneer in the study of insect immunity, using the model organism Drosophila to decipher the mechanisms of innate immunity in animals. The initial insectarium facility has no BSL3, thereby limiting experiments to drosophila and rodent malaria parasite, P. berghei. A particular strength is the new insectarium which will enable exciting new research into vectors and agents of human disease (such as Mosquito transmitted dengue virus).

Weaknesses and risks linked to the context

The technical resources are crucial but quite insufficient for the expected developments, notably inside the insectarium; we therefore advise the body institutions to bring as many technical people as feasible.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy.

Strengths and possibilities linked to the context

Four main objectives are proposed for the next five years, all based on the unit's research strengths and considerable expertise. The proposed projects are original and world-leading and are expected to yield considerable new scientific knowledge. The collective expertise of the unit members is a major strength, but the proposed projects are also outward looking and involve many external collaborations with other leading laboratories. A particular strength is the new insectarium, which will enable exciting new research on vectors and pathogens of human disease. M3i is eager to implement some of its research findings in the near future and to conduct exploratory projects to identify new research priorities. For example, innate immune system responses to oncogenic cells will be investigated following the discovery of a strong transcriptional response of Drosophila to oncogenic cell injection. Overall, the research plans are clearly feasible within the proposed time frame, as many of the planned projects appear to be based on extensive preliminary work. Detailed strategies and complementary approaches should be discussed in the interviews.

Weaknesses and risks linked to the context

While the scientific and societal impact of the research is remarkable, the major weaknesses remain the lack of translational research, therapeutic and industrial applications. The document mentions the possibility that projects conducted by ERL Inserm have "obvious translational potential for the control of vector-borne diseases such as malaria or dengue fever," but no patent or project for vector control in an endemic country supports this claim.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets.

Strengths and possibilities linked to the context

The Laboratory Council (Conseil de Laboratoire) is the main administrative body of M3i, where each category of personnel (researchers, teachers/professors, technical/administrative staff, students) is represented by an elected member. In addition to the mandatory Laboratory Health and Safety Committee (LHS) with two safety officers, the unit has an Equal Opportunities Officer who actively participates in the CNRS and Inserm regional networks to promote gender balance. Most likely thanks to the "Gender Equality Plan" implemented by the Director, the ratio between women and men in the position of Team Leader at M3i is well balanced.

All these organs meet on a regular basis. This organization is transparent and well suited to the size of the Unit. The Institute organizes regular events contributing to scientific animation. There are specific meetings gathering students/post-docs or technical staffs where research is presented and discussed.

The unit applies all the necessary provisions for the protection of its scientific assets and computer systems. The website (https://ibmc.cnrs.fr/laboratoire/m3i/) seems updated and informative.

M3i and IBMC apply the recommendations to avoid environmental risks and pursue sustainable development goals through various measures. They also have a business continuity plan that proved effective in 2020 during the closure of Covid-19 to maintain fly and mosquito lines.

Weaknesses and risks linked to the context

The architecture of the unit lacks an external scientific advisory board. The director should be assisted in his scientific management by an external SAB, which, although not mandatory, is usually present in other CNRS and Inserm units.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The M3i unit maintains an excellent attractive scientific reputation because of its outstanding research in the field of Drosophila and now mosquito immunity.

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area.

Strengths and possibilities linked to the context

The M3i unit benefits from a long history and record of outstanding research in the field of Drosophila and now mosquito immunity. As such, the unit has maintained an attractive scientific reputation, which resulted in the participation by some of the unit members (especially seniors) in 48 national and 126 international seminars, symposia, conferences, congresses, etc… Members of the unit were not only invited worldwide to events restricted to insect immunity but also presentations were made in forum of wider scientific interest. Senior members of the unit were also active in organizing meetings and conferences attractive to the international scientific community (French Academy of Science, Jacques Monod, XIVth BioMalPar as examples). The participation in European projects (infect-ERA, two H2020 projects and one UFA project) grants to the research unit scientific attractiveness and contributes to the construction of the European research area. Four senior members of the research unit were, during the period of evaluation, on the editorial board of six recognized journals (*Developmental and Comparative Immunology, Cell Host & Microbes, PLoS Neglected Tropical Diseases, Scientific Reports, Immunogenetics and Fly*). Besides, members of the M3i are evaluators for projects for important funding bodies such as NIH/ NIAID or EMBO. At the national level, the director of the unit has important roles of (1) assessment in the French National Assembly through OPECST, (2) presiding the Scientific advisory board of the International Center for Research in Infectiology (CIRI), (3) chairing one Hcéres evaluation committee or (3) presiding the section 27 of the National Committee on Scientific Research (CoNRS). In top of influencing national scientific policies and orientations of important scientific bodies, these activities also reflect the reputation of the M3i unit at the national and international context. The Emeritus J. Hoffmann is involved in many juries for academical prizes and sits on the scientific and administration boards of several national and Chinese institutions warrant publicity and visibility for the M3i research unit. Also, four of the M3i scientific staff were awarded with renowned national and international prizes. Membership of recognized scientific academies and institutions were not left behind (US National Academy of Sciences, French Academy of Sciences, EMBO, Institut Universitaire de France and others).
The major attractiveness is and will be the possibilities offered by the new insectarium, which allows to develop projects on vector mosquitoes and human pathogens.

Weaknesses and risks linked to the context

There is no major weaknesses. However, attendance and presentation of work in seminars, symposia, conferences, congresses (oral presentation, poster awards, etc.) by PhD students, post-docs and other non-senior members of the research unit are not mentioned in the Self-Assessment document. They also contribute to the reputation of the M3i unit and to the construction of the European research area.

2/ The unit is attractive for the quality of its staff hosting policy.

Strengths and possibilities linked to the context

Without doubts the M3i unit attracts national and international young research fellows (33 PhD students and 17 post-docs for the period evaluated). The research unit takes care for newcomers to help on the administrative burden linked to the installation of young scientists, in particular foreigners. This favors since the beginning a relation of trust between the newcomer and the research unit. Office space with personal desks and computer is provided for each junior scientist; this is not always the case in other research units or institutions. Apparently, there is no differences between young, seniors, permanent staff or contracted personnel concerning access to resting areas or research facilities. Young researchers are sensitized to issues as research integrity and open science with dedicated training. Good practices, as information to the director of publications prior submission seems to be respected. All students are followed annually by an advising committee issuing a report. Weekly seminars are dedicated to the advancement of work performed in the unit. In addition, given the academic and technical track of the permanent staff a quality supervision of junior scientists is insured. The M3i research unit exploit all available opportunities to incorporate junior or senior scientist or to provide them a solid background to apply for external tenure track positions. In the same way, two associate professors have been promoted to full professors. One post doc obtained a permanent position at CNRS and others are applying. Two technical staff were promoted assistant-engineer and engineer. This is the reflect of a dynamic unit, although having an important turn-over of personnel (PhD, post-docs, contracted staff) can still maintain a very high scientific level with attraction to junior and less junior scientists.

Weaknesses and risks linked to the context

No major weaknesses have been observed. Construction of the new insectarium and the COVID-19 pandemic were not favorable for visiting scientists but the situation is changing. Hands on trainings are not offered or widely advertised to external specialists in the form of workshops or on demand training.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects.

Strengths and possibilities linked to the context

The M3i unit successfully gets funding from the international, European, national, and regional grants (e.g., NIH, EU-H2020, ANR, Marie Sklodowska Curie and Regional Grand-Est). The high rate of success in terms of ANR funds obtained is impressive (11 ANR grants, 7 of them as coordinators). Furthermore, the unit received financing from Labex NetRNA, which has recently been renewed and get funding from Equipex program I2MC, which allowed to get equipment for the new insectarium.
Twelve post-doctoral fellows from different countries (France, Germany, Italy, Portugal, India, China, Japan, Brazil) were attracted due to their own financing and the excellence of the unit, which it is noteworthy considering the COVID crisis and insectarium transition. The M3i unit will undoubtedly benefit from the funding for the IMCbio graduate school due to the connection between the excellence research conducted in the M3i unit and education provided through targeted initiatives at both the Master's and PhD levels.

Weaknesses and risks linked to the context

No specific weaknesses or risks concerning the recognition gained through success in competitive calls for projects was identified. However, it is noted that there is a lack of highly competitive European grants (e.g., ERC).

4/ The unit is attractive for the quality of its major equipment and technological skills.

Strengths and possibilities linked to the context

The M3i, within the IBMC has largely contributed to create a state-of-the-art insectarium. The insectarium has BSL3 and BSL2 areas and are packed with up-to-date equipment, some of them tailored to specific needs (i.e., incubation glove box to manipulate mosquitoes infected with pathogens that need high containment level). Full list of equipment and distribution of working areas are well described in portfolio 1. With no doubt this infrastructure is one of the kinds in Europe. Special mention of excellence should be awarded to one engineer for her involvement in the phase of construction and now managing the infrastructure despite problems in getting permanent supporting staff. Scientific staff uses other platforms of IBMC and notoriously, the insectarium got the IBISA label allowing to apply for the purchase of new equipment. Therefore, the insectarium is on open access to external users with an extended list of services very well described in the IBISA web site. Good internal use of the insectarium is shown by seminal publications on mosquitoes infected by dengue or Zika viruses or *Plasmodium* parasites. These publications highlight technologies (transgenesis to cite only one) offered to the scientific community. From the quality of the research unit output, it is apparent that the technical staff is very well trained and motivated. Scientists have now an exceptional tool to tackle major biological problems on insect immunity and infection relevant to public health. Research on *Drosophila*, the flagship of the unit, has been facilitated by the new insectarium with a dedicated space. The Director and senior staff are still struggling and fighting to get permanent staff to manage the insectarium.

Weaknesses and risks linked to the context

Services are not advertised beyond the CORTECS or IBISA web sites, outreach potential international users is not completely achieved. The infrastructure is not currently staffed properly with permanent positions and could have negative repercussions on the unit performance.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the M3i unit is excellent.

1/ The scientific production of the unit meets quality criteria.

Strengths and possibilities linked to the context

The scientific output of the M3i unit in the years 2017-2021 has been excellent producing manuscripts of high quality. In the evaluation period scientists from the unit signed 57 primary research papers and 18 reviews with about 2/3 reporting work originating from the unit with members signing as first or leading authors. Although the quantity of published reseach papers is relatively modest considering the unit's size, several of these manuscripts were published in top tier journals of broad interest (*Nature, Nature Microbiology, PNAS, Cell Host & Microbes, Mol. Cell, Immunity, Cell reports, EMBO reports, PLoS Pathogens*).
The reported findings comprise breakthrough discoveries in line with the research interest of the unit and include the finding of a novel evolutionary conserved resilience mechanism in enterocytes (*Cell Host & Microbes*), the impact of the RNAi pathway on dengue and Zika virus dissemination in the insect host (*Nature Microbiology*), the role of proteases in activating innate immunity (*Molecular Cell*) as well as highly innovative topics such as the recognition of cancer cells in drosophila (*PNAS*) or the characterization of novel pattern recognition receptors in drosophila (*Nature*).
The unit has developed a strong in house insect related technical expertise (dsRNA injection, CRISPR:Cas9, fluorescence reporter) used as resource for several projects (e.g. for the generation of transgenic mosquito lines). This technical expertise is internationally recognized through collaborations and joint publications with renown international experts. The new insectarium has expanded the research perimeter to level 2 & 3 human pathogens and their insect hosts resulting in innovative and high-risk themes (e.g., development and implementation of drug and genetic based antiviral and anti-parasite strategies).

Weaknesses and risks linked to the context

No specific weaknesses concerning the quality criteria of the scientific production was identified. The new insectarium is considered an asset for the high quality of the scientific production. One potential risk for the unit is shortage of trained technical staff to make full use of the possibilities that the insectarium offers.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel.

Strengths and possibilities linked to the context

The M3i unit has a strict policy to prioritize publication quality over quantity. This policy is reflected both in the high quality of the scientific output but also in the overall productivity of its members during the evaluation period, covering all 4 research topics investigated in the unit. All tenured researchers, professors and the majority of contractual members (postdocs and Ph. Students) of the M3i unit contributed to the overall scientific productions (i.e., as named author and/or by providing a conference contribution or seminar).

Weaknesses and risks linked to the context

The unit is presented as team but clearly divided in 7 identified research groups (https://ibmc.cnrs.fr/laboratoire/m3i/) with some imbalances in the contributions between groups to the overall scientific production.
Furthermore, more than half the Ph.D. students leave the unit without a first author paper. Specific procedures for publications strategies concerning young researchers are not mentioned. The committee appreciates the objective to delay publication for the sake of quality but reminds that first author publications are an important part of a young researcher career.
Although the quality of the scientific production is high, the unit's output in terms of quantity of published papers is relatively modest considering the unit's size.

3/ The scientific production of the unit complies with the principles of research integrity, ethics and open science.

Strengths and possibilities linked to the context

The M3i unit is in compliance with established CNRS, Inserm and Unistra rules on scientific integrity and open science. To implement these rules, Ph.D. students have to follow online modules for scientific integrity provided by the Doctoral School and new members of the unit are instructed to follow good laboratory practices and sign a confidentiality Charta.
Each member of the unit presents his work in progress seminars with the goal to achieve the highest standards in scientific rigor and quality. Scientific data are recorded in electronic form. Data are daily secured on external hard drive while Inserm researchers of the unit use an electronic lab book managed by Inserm. Projects that are considered final are electronically locked but can be traced to individual contributors.
M3i complies with open science and all accepted manuscripts are available through the open access platform of the university of Strasbourg.
M3I complies with rules and standards concerning human life. All use of human samples (i.e. blood samples for feeding or infected samples) have obtained authorization from ethics committees in France or the country of residence of the donor. The work with genetically modified organisms was agreed following review by the HCB and delivered by MESRI.

Weaknesses and risks linked to the context

No specific weaknesses or risks concerning the scientific integrity was identified.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

The inclusion of the unit's research in society is excellent.

1/ *The unit stands out by the quality of its non-academic interactions.*

Strengths and possibilities linked to the context

The laboratory conducts major fundamental research in the fields of innate immunity and host-pathogen interactions with specific economic and societal actions. The characterization of antimicrobial effector mechanisms using model insects is particularly well adapted to identify novel antibacterial, antifungal or antiviral molecules, conducting to innovative strategies to fight major infections that are nationally and internationally priorities. Furthermore, in a context of global changes including climatic warming, mosquitoes are important vector species for parasitic and viral diseases and constitute crucial targets for the control of major vector borne diseases continuously progressing affecting human health and economy.

The laboratory is clearly identified by national scientific and governmental organizations due to excellent quality of the research demonstrating the high skills in major environmental and diseases concerns.

The laboratory contributed to various national expertise, as expert for Haut Conseil des Biotechnologies (HCB) with HCB's 2017 "Advice on the use of genetically modified mosquitoes for vector control", and for ADEGE to provide recommendations regarding the use of bio-insecticide *Bacillus thuringiensis* for mosquito control in France.
Major contributions, to meetings of representatives of National Assembly (OPECST) in the frame of discussions on new technologies, testified in front of a National Assembly group to inform them on the mosquito vectors and strategies to limit disease transmission, and participated to a discussion on sustainable development with the Minister of Higher Education, Research and Innovation have been conducted by several scientists.
The laboratory has also been involved in a scientific report on insect decline for the G7 Economic Summit and for national policies and a scientist is also a member of citizen group to advise local policies on Covid-19.

Weaknesses and risks linked to the context

No real weaknesses and risks have been identified.

2/ *The unit develops products for the socio-economic world.*

Strengths and possibilities linked to the context

During the evaluation period, the laboratory established an important collaboration (2754 k€; 2018-2021) with the Chinese company Infinitus, with the goal to develop therapeutics based on traditional Chinese medicine. The evaluation of polysaccharides on microbiota and gut host defense and resistance to viral infections but also the elucidation of the mechanisms of action using the *Drosophila* model have been conducted. A collaboration request from GlaxoSmithKline has also been registered.

Novel anti-malarial drugs under development in collaboration with another group will be patented soon. In addition, it is important to note the development of exploratory projects to identify a strong transcriptional response of *Drosophila* to the injection of oncogenic cells, highlighting the reactions of the innate immune system to oncogenic cells with high potential valorizations.

To facilitate the development of other collaborations but also generate resources to contribute to the maintenance of the recently constructed and IBiSa certified insectarium, this infrastructure is positioned as an open platform to academic laboratories and private companies. The laboratory has made the insectarium BSL3 facilities available to a private company Biosynex for the development of COVID-19 test kits during the pandemic.

Weaknesses and risks linked to the context

Several PhD students have benefitted from partial funding of their doctoral contract from the Grand-Est Region but no financial support in collaboration with private company has been obtained. Laboratory must try to obtain other financial support like Cifre (Conventions industrielles de formation par la recherche; Industrial training agreements through research) for PhD students indicating close collaboration with private companies. Laboratory develops high-level research with numerous applications in societal and economic topics that should reinforce interactions with private companies and/or protective actions of the results with patent deposits.
Only one contribution is in progress for intellectual property on antimalarial drugs. Invention disclosures need to be strengthened in this context to amplify patents filings or other protective actions. This could also open new opportunities to interact with private companies and/or create start-up.

3/ The unit shares its knowledge with the general public and takes part in debates in society.

Strengths and possibilities linked to the context

The laboratory is highly active, using various supports (conferences, TV, radio, press, Internet) to explain and disseminate knowledge, research results and ethical issues through vulgarization to a large audience. Scientists from the laboratory participate to various events such as Fête de la Science, Forum Européen de Bioéthique.
A science sketches video freely accessible on internet, introducing the principles of antiviral RNA interference has been developed during the lockdown in the spring 2020. Numerous public conferences or exhibitions about mosquito-borne diseases and/or how genetically modified mosquitoes could be used in vector control / disease control strategies have been conducted by the laboratory during the period. The laboratory is also involved in the scientific advisory board of the Strasbourg Zoological Museum to provide advice on the design and contents of its new permanent exhibit on insects, with a focus on bees and research on vector mosquitoes. Furthermore, a partnership with Maison des Sciences regularly mobilizes the laboratory to interact with biology teachers and explain them new mosquito-related technologies as well as provide them practical and theoretical knowledge of vector-borne diseases. The laboratory also directly interacts with classes during specific events (conferences, speed meetings). Scientists from the laboratory organize workshops for schoolteachers, including a visit of the laboratory and insectarium and the production of pedagogic kits for their pupils. Declics ambassadors from laboratory allow interactions between scientists and high school students. In this context, a film for high school students shown to enrolled classes, with live response to pupils' questions has been produced and is in free access to internet. The laboratory gave seminars to school classes and welcomed high school students for their supervised practical works on mosquito research.

Weaknesses and risks linked to the context

No real weaknesses and risks have been identified. The laboratory well managed the various actions. It is important to maintain a good balance between laboratory members to manage the different scientific dissemination activities. Social scientific networks and social marketing should also be efficient ways of scientific dissemination to inform a large audience (particularly sensitive during crisis).

C - RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, resources, and organization of the unit

The ERL is a valuable asset to the unit. It provides extra human resources through Inserm with tenured scientific positions and technical/funding support. This collaboration between the CNRS and Inserm should be continued in the next term.
The expert committee recommends reorganization of the unit's single team organization into a multi-team one with a clear focus on highly innovative and leading-edge topics.

Recommendations regarding the Evaluation Area 2: Attractiveness

The participation of PhD students and post-docs in international and national congresses should be encouraged because they are the future for the construction of the European research area.
The expertise of the unit should be shared with the Scientific community by organizing workshops hand-on in the new insectarium. The services offered by the unit should be beyond IBISA and Cortecs platforms to open it to external academic and industrial users and promote scientific collaborations with other research institutes.
The lack of success to obtain ERC Advanced grants or Human Frontiers Science Program grants on *Drosophila* should not demotivate the researchers to try it again using the knowledge generated at SFHI. European funding will be easier to get with proposals on novel strategies to control mosquito borne viruses or parasites.

Recommendations regarding Evaluation Area 3: Scientific Production

The expert committee recommends *ensuring that there are funds to support key technical staff to make full use of the opportunities offered by the new insectarium.* Although the quality of the scientific production is high, the unit's output in terms of quantity of published papers is relatively modest considering the unit's size.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

Laboratory develops high-level research with numerous applications in societal and economic topics that should reinforce interactions with national, European and other international private companies. Industrial PhD training agreements through research should be developed. Invention disclosures need to be strengthened to amplify protective actions of the results with patent deposits.

CONDUCT OF THE INTERVIEWS

Date

Start: 19 October 2022 at 09:00

End: 19 October 2022 at 18:30

Interview conducted: online

INTERVIEW SCHEDULE

9h – 9h30	**Hcéres committee meeting** *Closed-door meeting*
9h30 – 9h35	**Hcéres rules and procedures by J. Dutrieux** *Public session (all unit members)*
9h35 – 10h35	**Administrative and scientific presentation of the unit's achievements and future by J-L. Imler and S. Blandin** 40min presentation 20min discussion *Public session (all unit members)*
10h35 – 11h	**Committee debriefing and pause** *Closed-door meeting*
11h – 11h30	**Meeting with ITAs (*in French*)** *In the absence of managing staff*
11h30 – 12h	**Meeting with researchers** *In the absence of managing staff*
12h – 12h300	**Meeting with PhD students and postdoctoral fellows** *In the absence of managing staff*
12h30 – 13h20	**Lunch pause**
13h20 – 14h00	**Meeting with institutions representatives** *Closed-door meeting*
14h – 14h30	**Committee debriefing** *Closed-door meeting*
14h30 – 14h45	**Pause**
14h45 – 15h15	**Meeting with the unit director** *Closed-door meeting*
15h15 – 15h30	**Pause**
15h30 – 18h30	**Redaction of the final report** *Closed-door meeting*
18h30	**End of the interview**

GENERAL OBSERVATIONS OF THE SUPERVISORS

Université de Strasbourg

Monsieur Éric Saint-Aman
Directeur du Département d'évaluation de la recherche
HCERES - Haut conseil de l'évaluation de la recherche et de l'enseignement supérieur
2 rue Albert Einstein
75013 PARIS

Strasbourg, le 5 juillet 2023

Objet : Rapport d'évaluation DER-PUR230023298 - M3I - Modèles insectes d'immunité innée

Réf. : RB/FF/ 2023-450

Rémi Barillon
Vice-Président Recherche, Formation doctorale et Science ouverte

Affaire suivie par :
Florian Fritsch
Responsable du département Administration de la recherche et accompagnement des chercheurs
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Cher Collègue,

L'université de Strasbourg vous remercie ainsi que tous les membres du comité HCERES pour le travail d'expertise réalisé sur l'unité de recherche « Modèles insectes d'immunité innée » (M3I – UPR 9022).

Nous n'avons aucune observation de portée générale à formuler sur le rapport d'évaluation transmis.

La tutelle CNRS nous a indiqué qu'elle ne s'exprimerait pas sur le rapport d'évaluation à ce stade.

Je vous prie d'agréer, Cher Collègue, l'expression de mes cordiales salutations.

Rémi Barillon

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