

EVALUATION REPORT OF THE UNIT
CardioVir - Viral cardiovascular infections and
inflammation in human pathology

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université de Reims Champagne-Ardenne -
URCA

EVALUATION CAMPAIGN 2022-2023
GROUP C

Report published on March, 22 2023



In the name of the expert committee¹ :

Michael Schindler, Chairman of the committee

For the Hcéres² :

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 Michael Schindler, University Hospital Tübingen, Germany

Experts: Ms Claire Deback, Université Paris Saclay (representative of CSS Inserm)
Ms Christine Goffinet, Charité - Universitätsmedizin Berlin, Germany
Ms Jennifer Molle, Inserm, Lyon (supporting personnel)
Mr Patrice Morand, CHU Grenoble (representative of CNU)

HCÉRES REPRESENTATIVE

Ms Birke Bartosch

CHARACTERISATION OF THE UNIT

- Name: Viral cardiovascular infections and inflammation in human pathology
- Acronym: CardioVir
- Label and number: EA-4684
- Composition of the executive team: M. Laurent Andreoletti

SCIENTIFIC PANELS OF THE UNIT

SVE4 Immunity, Infection and Immunotherapy

THEMES OF THE UNIT

CardioVir has an ongoing research program concentrating on viral cardiovascular infections and inflammatory responses in human pathology. They study the molecular mechanisms of cardiomyopathies induced by these infections. More specifically, how enteroviruses are involved in developing the inflammatory response during acute and chronic infection and the modulation of the type I interferon response. More recently, they also implemented work on SARS-CoV-2.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

CardioVir was created in 2012. It belongs to the Medical Faculty of Reims of the University of Reims Champagne-Ardenne (URCA) and is located (250m) nearby the Academic Hospital of Reims.

RESEARCH ENVIRONMENT OF THE UNIT

The CardioVir is integrated into the SFR-Cap, Santé research structure since 2018 with the goal to promote a coherent strategy in basic research. Here, the unit belongs to the "health and environment" axis and the "infection and inflammation" theme. The director and vice-director are members of the SRF-Cap Santé board.

The unit has a proprietary research lab area of 246m² and 70m² of office space. They have access to various omics techniques and platforms including flow cytometry, animal facility, confocal and electron microscopy. Currently, BSL3 lab space is shared with bacteriologists and the diagnostics facility. A new BSL3 is build and shall be implemented soon. All of the 7 HDRs have clinical duties and are involved in medical care and diagnostics with formally 33% of working hours allocated to research. The unit has one full time researcher, a postdoc and a research technician, both employed at 100%, as well as a shared secretary. The unit is labelled a university research team. There is no restructuring or fusion planed or scheduled.

By giving 5% of its funds coming from the university to the SFR-Cap Santé the unit has access to several state of the art facilities including the Biological Resource Center, animal facilities, tumor libraries, imaging platforms and many more.

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

Permanent personnel in active employment	
Professors and associate professors	7
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	0
Scientist (Chargé de recherche, CR) and associate	0
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	7
Subtotal permanent personnel in active employment	14
Non-permanent teacher-researchers, researchers and associates	1
Non-permanent research supporting personnel (PAR)	0

Post-docs	0
PhD Students	3
Subtotal non-permanent personnel	4
Total	18

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

Employer	EC	C	PAR
Université de Reims Champagne-Ardenne	4	0	4
CHU Reims	3	0	3
Total	7	0	7

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	108
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	155
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	195
Own resources obtained from international call for projects (total over 6 years of sums obtained)	176
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	125
Total in euros (k €)	759

GLOBAL ASSESSMENT

CardioVir performed highly original research in the field of enteroviruses/cardiomyopathies with international visibility. The unit published a set of 6 remarkable papers establishing the role of 5' UTR deleted enteroviruses in the pathophysiology of myocarditis and several others concerning pathogenesis and mechanisms of cardiopathophysiology in enterovirus infection. In the Covid pandemic the unit supported the regional (Champagne-Ardenne) need for SARS-CoV-2 molecular diagnostic assays (two contracts with private medical consortia (BIOXA and UNILABS)). CardioVir did good research in the Covid-19 pandemic. If this will become a sustainable future line of research in this highly competitive field is a matter of ongoing development.

There is excellent support from URCA in terms of funding for personnel and a BSL3 for CardioVir is currently under construction. The BSL3 will offer excellent opportunities for upside potential to increase fee-for-service and third party funding in order to strengthen and further develop the research capacity within CardioVir.

As already stated, there is very good scientific productivity on enterovirus subjects. The unit bridges basic to clinical research in an excellent manner with the potential of knowledge transfer to establish new immunobased therapeutics for the treatment of cardio-viral infections. Hence, the HDRs that have been occupied in the last years by clinical duties related to the Covid19 pandemic, should engage more intensively on their research mission, such as that Cardiovir can lever its existing potential.

In recent years, the unit increased research staff as a 100% researcher and research technician were recruited, as well as a postdoc. Here, efforts should be undertaken to prevent a brain drain and maintain as well as expand staff involved in research. In this context, it is noteworthy that the team is very well managed. There seems ongoing and fruitful scientific discussion that also involves the clinicians with bi-weekly overall team meetings to discuss scientific and organizational issues, as well as individual meetings of the director/co-director with the research members. Given the international visibility and networking activity of the director, the prospects and the team spirit, more MSc students, PhD students as well as post-doctoral researchers and young HU medical

virologists could and should be attracted. CardioVir established and expanded collaborations with immunologists from the Institut Pasteur in Paris, Strasbourg and Nancy, which is an essential pre-requisite to be successful in their research focus, since locally there is a weakness in antiviral immune response expertise.

The unit has significantly increased its public outreach, particularly in respect to its activities on SARS. For CardioVir this opens the opportunity to also start outreach activities in previously neglected topics to also raise awareness in their core focus area concerning enterovirus infections of the heart and the associated cardiopathologies.

Overall, the board judges the performance of CardioVir over the last five years very good to excellent with exciting opportunities of further development.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

In response to the recommendations from the previous evaluation, the unit strengthened the research personnel and hired one 100% researcher PhD and a 100% research technician. Furthermore, a postdoctoral researcher was recruited with support from the URCA.

To increase collaborations on the national level in immunology CardioVir engaged into a partnership with the Pasteur Institute in Paris to identify 5' truncated viruses and with Sorbonne University. In the topic of epigenetics CardioVir collaborates with University of Nancy Grand Est and in innate immunology with the University of Strasbourg.

A persistent recommendation of the previous evaluation was to increase involvement of clinical personnel with HDR in training of students and in the development of the research of the unit. Even though some of the HDRs seem to participate in research, there is still enormous potential to drive this further, and the committee does not see any specific initiatives taken during the last years to improve this. On the other hand, this might be explainable by the high demand on clinical diagnostics and patient care during the Covid pandemic.

B - EVALUATION AREAS

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

Assessment on the unit's resources

The unit has good to very good success in funding leverage.

Assessment on the scientific objectives of the unit

The scientific objectives related to enteroviruses are excellent, good to very good for other viruses.

Assessment on the functioning of the unit

The functioning of the unit and 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

CardioVir is embedded in a very fruitful scientific environment and the research facilities sustain the activity profile of the unit. The unit succeeded to hire a full-time researcher and technician fostering their research activities and the unit is strongly supported by URCA to finance staff.

The unit has successfully applied for third party funding, representing €774K in five years, ~155k€/year.

The unit has access to 246 m² lab space, with platforms of the SFR Cap-Santé (L2, Cytometry, A2 standard and KO animal facility, confocal microscopy and electron microscopy) and to the innovative biology platform (PRBI) of the biology department of the Academic Hospital of Reims (Sanger sequencing, NGS, proteomic), and 70 m² office space. A new BSL3 is currently under construction funded by URCA. This is an excellent opportunity for the research of CardioVir. The BSL3 structure will be academic with a good visibility in the Champagne Ardenne area, and forms a basis for CardioVir to develop collaborations with local or national industrial partners.

Staff-wise, the unit is composed of 21 members, comprising the director and the deputy director, researcher-physicians, hospital practitioners, one full-time researcher, several PhD students, one postdoc, a research technician and a shared secretary (0,25 FTE).

The HDRs that are involved in clinical work link basic to clinical research, this facilitates translational aspects and research with patient cohorts.

A relatively high proportion of highly experienced scientists creates a perfect environment for PhD training.

Weaknesses and risks linked to the context

Given the size of the unit (21 members in total), one research technician appears not enough. Also, it is surprising that there are only 3 PhD students (as of 31st of December 2021). €774K third party funding in five years seems limited to sustain the ambitions of the unit. There is no research personnel employed based on external third-party funding.

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

Strengths and possibilities linked to the context

The unit's scientific objectives focus on a better understanding of the pathogenesis and innate immunity in the context of cardiotropic viral infections. It has established a multidisciplinary team covering experts in infectiology, virology, cardiology, forensic pathology, medical intensive care, cardio-thoracic surgery and ophthalmology. The unit also was involved in response to the Covid pandemic - it developed diagnostic tests and performed clinical research on Covid19 (screening, typing).

The unit allocated 5% of its annual resources to promote collective research activities and the emergence of innovative themes, allowing, among others, the development of a BSL3 laboratory project and the renewal of A2 accreditation in infectiology (new autoclave, revised ventilation). These developments will fuel research on cardiotropic viruses in the future.

The unit has strong local and national collaborations with institutional, academic and non-academic partners and at the societal level. At the national level CardioVir engaged into a partnership with Pasteur Institute in Paris to identify 5' truncated viruses and strengthen its research on immunology with Sorbonne University. CardioVir collaborates on the topic of epigenetics with University of Nancy Grand Est and in innate immunology with the University of Strasbourg. Joint ANR grants were submitted. There are industrial collaborations with for example BioMérieux.

Weaknesses and risks linked to the context

The unit has a clear focus on cardiotropic enteroviruses and the pathophysiology as well as mechanisms of causing inflammation and cardiomyopathy. There is a certain risk that this exciting niche is diluted by working on other pathogens as for instance arboviruses and SARS-CoV-2, which is a very competitive area. The implementation of the BSL3 might further fuel the dilution of the main theme.

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 onboarding strategy for new unit members is professional and quite all-encompassing. New unit members receive a training in good scientific practices.

The unit organizes a general lab meeting twice a month in which unit members (MSc/PhD students, postdoctoral researchers) present their research and organizational topics are discussed as well as the unit social life in organized. The unit states to be committed to respect gender equality and absence of discrimination, interdisciplinarity and welcoming of foreign members. The unit has internal rules and a charter delivered to each young researcher. The director and the vice-director as well as the unit council pay specific attention to the integration of each new member of the laboratory. It is recommended to each member of the unit to keep their vaccinations valid and each member benefits from a medical check-up at the occupational health department of Reims. Regarding doctoral fellows, the progress of their thesis and the potential scientific barriers are evaluated and discussed internally and externally during the thesis committees. About the management of infectious and laboratory risks, each newcomer undergoes a health and safety training course given by the unit's statutory "health and safety" referent (Tech URCA). The researchers are encouraged to save the data of

their project on a secured internal server (NAS type) which is implemented by CardioVir. The NAS server located at CardioVir is itself backed up in real time on URCA' SSD server. Access to the NAS or SSD of URCA is protected by a firewall and anti-hacking security systems. All computers are monitored for software maintenance by the university's IT department, with software updates and protective measures including UPS systems with a 6-hour power outage capacity. The director of CardioVir has the rights and access codes to all the backups on the NAS and the SSD of the URCA. The unit has implemented policies for energy saving and waste reduction.

Weaknesses and risks linked to the context

The management only encourages unit members to save-guard their data on the internal server. However, there should be mandatory rules to save-guard the data and official SOPs to save on the internal servers that are backed-up.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The work on enteroviruses is very good to excellent, it is too early to evaluate the work on SARS-CoV-2.

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

CardioVir is well recognized for the quality of its research, its expertise and skills in cardiovascular pathology of viral etiology at national and international levels. It keeps its originality and specificity as a scientific niche in the field of cardiovascular viral infections and the unit possesses international competences on identification of the viral causes of sudden cardiac death and in the physio-pathological exploration of unexplained causes of hospitalized or fatal myocarditis in infants or young adults.

CardioVir is a single and monothematic team. It gathers multidisciplinary experts in virology, forensic, pathology, cardiology, cardiothoracic surgery, ophthalmology and infectious diseases. The organization of multidisciplinary skills around a single research theme is a strong point.

CardioVir has a long-lasting national and international academic reputation. It benefits from fruitful international collaborations with US leaders in the fields of molecular biology of *Picornaviruses* from Nebraska University and UC Irvine CA USA. A post-doctoral grant from the Hewitt Irvine Foundation USA has been awarded to a PhD student in the CardioVir-EA 4684 laboratory, in the framework of a partnership with a collaborator at Irvine, UCI (International contracts as a partner 2016-2020).

The unit is implicated in the construction of the European research area. Between 2018 and 2021, CardioVir developed new collaborations in France with Paris Pasteur Institute (Institute of Virology, Viral Genomics and Vaccination Unit), Paris Sorbonne University (IBPS, CNRS UMR 8256, Biological Adaptation and Aging), the University of Nancy Grand Est (Biochemistry and platform of Epi-RNA-Seq IMOPA), and the University of Strasbourg (Innate immunology and antiviral immunological response in insects).

CardioVir has collaboration with The French Enterovirus Myocarditis Study Group (FEMSG), as well as the Centre National de Référence (CNR) des Entérovirus et Parechovirus (Lyon).

Members of CardioVir presented their work in 9 international conferences including, 2 in the US and 3 in Europe via ESCMID conferences.

The director and one researcher of the unit are members of the scientific board of the European Society of Microbiology and Infectious Diseases (ESCMID).

Weaknesses and risks linked to the context

There is no mention of a European research network on myocardial viral infections, which could be developed by the unit given its reputation.

No AHU / MCU PH is present in the unit.

The website of the unit provides only limited information on its activities and is not up to date.

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

Strengths and possibilities linked to the context

CardioVir is located at 250 meters from the Academic Hospital of Reims. This proximity favors scientific projects between basic and translational research in viral cardiovascular infections and inflammatory response in human pathology.

The unit has hired two permanent positions, a research technician in 2018 and a research engineer in 2020 (URCA).

CardioVir welcomed three post-doctoral researchers; one of whom became a statutory member on a full-time position of local (URCA) university research engineer in 2020. This post-doctoral researcher came back from her second post doc in the USA (2016-2017, Scripps Research Institute, Florida, USA) to take up her position as an URCA research engineer in the unit. She obtained her definitive statutory position (Research engineer) in June 2019.

The unit welcomed 7 PhD students during the present evaluation period, 4 of whom defended their thesis during the last 5-year period. These 4 PhDs have all signed articles as first or co-first author.

Between 2016 and 2021, the unit welcomed also 4 Master-1R and 7 Master-2 R students as well as two foreign students in 2015 and 2021 (medical students or MD in infectious diseases from Chad) in the framework of an inter-university collaboration agreement (URCA-CHUBS).

The unit is attentive to the working conditions of its staff, their health, safety and the prevention of psycho-social risks, paying specific attention to the integration of each new member of the team. Each PhD student signs several official documents including: a welcome charter, a confidentiality charter as well as a charter of respect and ethics of scientific data.

The vice-director of CardioVir is a member of the organizing committee of the Reims' days for young researchers in health and science fields (JRJCS).

Weaknesses and risks linked to the context

The strengthening of the research team with the recruitment of statutory researchers remains recent but should increase to produce results that can be published in journals with higher recognition status and that open the possibility of economic transfer in the field of viruses with cardiac tropism in humans (*Picornaviridae*, SARS-CoV-2...).

Links with immunologists remain recent. A permanent position in immunology is missing in the unit.

As already observed in the precedent evaluation (2016-2022), the unit director is involved in the training activities of nearly all hosted students (master projects) and supervises all the PhD students, albeit the presence of 7 HDRs in the team.

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

Between 2018 and 2021, CardioVir has been supported by the University of Reims Champagne-Ardennes (URCA), providing a recurrent funding of ~25 k€ per year.

The members of the unit have succeeded in obtaining institutional funding from the ANR (ANR-Flash Covid, 40keuros), PHRC (PHRC APHP AGEMOS, 40keuros) as well as funding from the Grand-Est Region for high-level researchers (15k€).

Weaknesses and risks linked to the context

The group recently applied for external third party funding including applications to the ANR (PRC, JCJC), however during the reporting period, its success in competitive grant leveraging was limited.

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

Strengths and possibilities linked to the context

Research area (246 m²) and offices (70 m²) are located within the faculty of medicine of the University of Reims Champagne-Ardennes (URCA).

CardioVir is fully integrated in the SFR Cap –Santé. The director and the vice-director are members of this SFR. The unit gives part (5%) of its own annual resources to promote collective research activities and the emergence of innovative themes.

CardioVir has direct access to the federative research structure (SFR) Cap-Santé and innovative biology platforms. The unit benefits from the facilities to conduct experiments in molecular biology (cloning, Crisper-Cas9 molecular engineering, high throughput sequencing with automated library preparation system), cell culture of human cells and production of modified or tagged prototype viruses by reverse genetics in BSL2.

Members of the unit have access to cytometry, proteomics, cellular and tissue imaging platforms and can rely on expertise in histology and immunochemistry on human and mouse cells and tissue.

The SFR includes the Biological Resource Centre and a tumour library.

The ROMEO computing centre provides researchers with high-performance computing resources, secured storage spaces, as well as support in the use of bioinformatics tools and softwares.

Importantly, innovative research on emerging viruses and future projects on cardiotropic viruses (CVB3 model) will be developed in the BSL3, which is currently under construction. The inauguration of this new scientific structure is scheduled for the end of April 2023.

The unit established a unique and valuable cardiomyopathy samples tissues collection.

Weaknesses and risks linked to the context

The BSL3, which is currently under construction, is also an important new infrastructure, however the committee sees a certain weakness in the proposed funding model for the running costs.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

Output is very good concerning enteroviruses and cardiovascular diseases.

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

Strengths and possibilities linked to the context

The role of "cardiotropic" viruses in acute or chronic cardiovascular disorders is an important topic to decipher and the CardioVir unit has developed for years a good scientific strategy allowing significant contributions to this topic.

This strategy is fully integrated within the scientific facilities and within the two axes of the federative research structure Cap Santé of the faculty of medicine: "Health/Environment" and "Infection and Inflammation".

The scientific output is good considering the size of the CardioVir unit, the number of full-time researchers and the narrow "scientific niche" of the main research topic of the unit. There is a sustained production from 2016 to 2021 of 48 articles with 44 original articles (including 7 case reports and 5 articles published in French journals) and with 4 review articles (including three in French journals).

Twenty-seven articles are related to the main research topic of the unit and a team member is involved as first or last author in 13 and 15 cases, respectively. Some of these data have been co-published with American teams and have been published in good to very good journals (*Emerging Infectious Diseases*, *Clinical Infectious Diseases*, *Journal of Virology*, *Circulation*, *Scientific reports*).

The main original scientific contributions from the unit during the 2016-2021 period were:

- (i) the demonstration of the role of truncated form of group B enterovirus during acute and chronic myocarditis and the impact of this new viral forms (also named RNA epitranscriptome of the virus) on the innate immune responses in the cardiovascular target cells.
- (ii) the improvement in forensic virology in the framework of sudden cardiac death in young adult and in the identification of viral causative agents of myocarditis in young people.

This has been facilitated by a good consideration of the recommendations of the previous Hcéres report (recruitments of research engineer and research technician, new collaborations with national experts in fundamental immunology of the antiviral response at Paris Pasteur institute, Sorbonne university and Strasbourg university).

This expertise could allow the unit to expand its research towards other human RNA viruses (e.g. SARS Cov2, influenza virus) involved in cardiovascular disorders. The future availability of a BSL3 facility starting in April 2023 in the faculty of medicine and the already existing collaborations with the Anglo-Saxon teams (UC Irvine California) will furthermore facilitate this.

During the period 2016-2021; 2 oral communications (American Society of Virology), 5 poster communications (American Society of Virology, European Congress of Clinical Microbiology and Infectious Diseases) and 3 invited lectures (European Congress of clinical Microbiology and Infectious Diseases) have been presented at international meetings in USA and Europe. The unit plans to present original results at international meetings in 2022.

Weaknesses and risks linked to the context

The scientific production of the unit appears rarely in high quality generalist journals.

Due to the size of the team and the international scientific competition about emerging RNA viruses, particularly the SARS-CoV-2, there is a risk to dilute the forces of the team if news themes are tackled.

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

Overall, the publication activity reported in the self-assessment document represents 2.82 articles per publisher and 9.6 articles per year. Seventeen out of the 20 staff members have published during the 2016-2021 period. The FTE calculated according to INSERM 2021 recommendations is 6.28. The mean number of articles per PhD student is 2.3. The PhD students who defended their thesis have all published in a first position (or co-first). The three post-doctoral researchers welcomed during the 2016-2021 period have published in international journals and one of them became a full time IGR of the unit and is currently the co-director of the unit

Of note, 8 publications out of the 48 reported are related to the SARS CoV 2 of which 3 are reported as belonging to the 20% most significant papers (n= 8) of the CardioVir unit.

Weaknesses and risks linked to the context

The average supervision rate of PhD students/HDR (0.28) is weak: only one HDR out of the seven has been in charge of the supervision of the seven theses of the 2016-2021-period.

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 unit has implemented excellent procedures to ensure that the scientific data comply with the rules and principles of research quality and integrity, particularly for the young students for whom the unit offers on one hand permanent training about scientific integrity and on the other hand regular checking of the data and experiments.

Each publication has been reviewed by the ethics committees for protection of human beings and animals.

The co- director of the unit is the referent of the respect of the principles of an open-science.

Weaknesses and risks linked to the context

No weakness to be mentioned.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

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

Involvement of the unit in the SARS-CoV 2 pandemic is very good to excellent, knowledge transfer and product development are good to very good.

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

Strengths and possibilities linked to the context

CardioVir developed non-academic interactions with charities, providing funds such as a ADETEC research grant (20k€) or from the French Federation of Cardiology (100k€). One post-doctoral researcher was supported by Hewitt Irvine Foundation Post-doctoral Fellowship (176k€).

In addition to that, CardioVir has participated locally to the screening and strain typing of SARS-CoV-2 and by training medical biologists.

The unit has produced a MOOC on SARS-CoV-2.

Weaknesses and risks linked to the context

No weakness to be mentioned.

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

Strengths and possibilities linked to the context

CardioVir developed industrial interactions resulting in grants from Gene Proof (35€) and Inodex (20k€). CardioVir also develops new diagnostics and therapeutics approaches in viral cardiovascular infections. A R&D project partnership(80k€) with bioMérieux for the research of peripheral biomarkers of viral myocarditis has been set up over the last four years and is expected to be continued during the next five-year research plan.

Weaknesses and risks linked to the context

No patents were filed, no licences were granted.

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 unit is involved in participatory science or citizen science activities through its funders such as the French Federation of Cardiology (FFC) or the Heart and Vessels Foundation or the URCA (University of Reims Champagne Ardenne) so that all non-scientists, and in particular patient associations can easily have access to the popularized data obtained by the scientific researchers of the unit.

The unit participated at the request of the URCA in communications or transdisciplinary conferences during the science festival in October 2021 on SARS-CoV-2.

The unit has regularly communicated on TV (n=3), radio (n=2) and in the press (n=10) on its virological diagnosis activities but also about the pandemic situation.

Weaknesses and risks linked to the context

No outreach activity concerning the core topic enteroviruses/cardiomyopathies was reported.

The unit's web site could benefit from an improved design.

C - RECOMMENDATIONS TO THE UNIT

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

We recommend that the co-director defends her HDR, which will give the unit the opportunity to increase the number of PhD students, thus contributing to the specific research profile of CardioVir. Furthermore, all other HDRs should intensify their research efforts as well as supervision of PhD students.

Funding for personnel is currently exclusively provided by URCA. To allow organic growth of the research (PhD students, post-doctoral researchers) the unit should attract more external funding through competitive grant applications (EC, ANR, ...) that also includes funding for salary of research staff.

CardioVir performs excellent research in the field of enteroviruses/cardiomyopathies and associated cardiopathology. If the unit aims to expand its research to other viruses, the research should align with the core techniques and the research focus on cardiotropic ssRNA viruses. For instance, to explore if other RNA viruses also evade innate sensing via 5' deletions and associated conserved mechanisms. The work on innate immune sensing should remain limited to this aspect and Covid19 research should be critically reviewed in light of the highly competitive nature of the Covid field.

Since it will be difficult to obtain ongoing funding for covering running costs for BSL3, the unit should continue discussion with URCA regarding institutional funding for the BSL3 infrastructure.

Recommendations regarding the Evaluation Area 2: Attractiveness

We recommend to recruit young hospital-university staff, both non-permanent (CCA-AHU), and permanent (MCU-PH), as this staff can take over teaching from the DU and reinforce translational and clinical research.

The post-doctoral position that will expire in 2023 should be renewed, as otherwise there will be weakening of the research area in the unit. We strongly encourage to intensify the ongoing exchange with URCA to install a chair for a junior professorship and to embed this position into the core research area of the unit.

To increase the visibility of the unit the design of its website could be improved and kept up to date and scientists might consider to get active in social media. This might ultimately attract more MSc students as well as PhD students to be trained and further foster research in the unit.

Recommendations regarding Evaluation Area 3: Scientific Production

We recommend that CardioVir intensifies its excellent research activities within its core expertise that is cardiotropic enteroviruses, ssRNA viruses and cardiopathophysiology as well as mechanisms of inflammation.

On all levels, that is research training, fundraising and implementation of research topics, especially in bridging basic to clinical science, the clinical HDR personnel should get more involved.

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

Given the strong translational research program of the unit and its potential in knowledge transfer, industrial collaborations could be enforced; CardioVir would strongly benefit from increasing its public outreach activity in the area of cardio-viral infections and associated risks.

As the new BSL3 offers various opportunities, we suggest to consider exploring opportunities of private-public partnerships. Such a measure might also lever sustainable fundraising for the facility.

CONDUCT OF THE INTERVIEWS

Date

Start: 15 septembre 2022 9am

End: 15 septembre 2022 18:30pm

Interview conducted: online

INTERVIEW SCHEDULE

Site visit agenda

- | | |
|---------------------|---|
| 9:00-9:10 | HCERES Rules and procedures by B. Bartosch
<i>Public Session (all unit members)</i> |
| 9:10-10:25 | Administrative and Scientific presentation of the Unit by the Director and the co-Director
10' L. Andreoletti, overall presentation of the unit
15' L Andreoletti, scientific achievements (part I)
20' F Berri, scientific achievements (part II)/ further scientific strategy
30' discussion
<i>Public Session (all unit members)</i> |
| 10:25-10:50 | Debriefing committee and break (<i>closed door meeting</i>) |
| 10:50-11:10 | Meeting with ITAs (in French)
<i>In the absence of any managing staff</i> |
| 11:15-11:35 | Meeting with researchers
<i>In the absence of any managing staff</i> |
| 11:40-12:00 | Meeting with post-docs and students
<i>In the absence of any managing staff</i> |
| 12:00-13:00 | Lunch Break |
| 13:00-13:40 | Meeting with institution representatives: URCA / INSERM (<i>closed door meeting</i>) |
| 13: 40-14:15 | Debriefing committee (<i>closed door meeting</i>) |
| 14:15-14:30 | Break |
| 14:30-15:00 | Meeting with the Director and the co-director of the Unit (<i>closed door meeting</i>) |
| 15:00-15:15 | Break |
| 15:15-18:30 | Redaction of the final report (<i>closed door meeting</i>) |
| 18:30 | End of the visit |

PARTICULAR POINT TO BE MENTIONNED

Pr Christine Goffinet has been unable to participate at the evaluation.

GENERAL OBSERVATIONS OF THE SUPERVISORS

Direction de la recherche et de la
valorisation

Affaire suivie par Karelle MASCRET
03.26.91.86.99

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Réf : 104 /RECH/NM/KM

Mr. President,

First of all, on behalf of all the researchers and teacher-researchers of the University of Reims Champagne-Ardenne, I would like to thank you for the time and energy you devoted to the evaluation of our research units. I would also like to thank you for the quality of the evaluation report and for the constructive exchanges we had with the HCERES committee. The recommendations and advice given as well as the interest shown in the future of our units will allow us to carry out our scientific project.

Following receipt of the HCERES report n° DER-PUR230022996 - CARDIOVIR - " Viral cardiovascular infections and inflammatory response in human pathology ", please find below the general observations of the unit: The HCERES international committee conducted a high quality evaluation of our unit during several visio-conference meetings during the day. We thank all the members of the committee for the quality of discussions and exchanges with the different category staffs of our unit. After reading carefully the proposed actual report, we have to notify several general remarks for the committee and the HCERES instances.

Our research topics are not focused only on Enterovirus infections and concerns also other cardiotropic viruses as recently SARS-CoV-2 and in the future other pathogens as Influenza or other emerging viruses.

During the COVID pandemic the unit supported the regional (Champagne-Ardennes) need for SARS-CoV-2 molecular diagnostic assays during the pandemic by two contracts with private medical consortia (BIOXA and UNILABS) and not directly the University Hospital Center of Reims.

"CardioVir unit established and expanded collaborations with immunologists from the Institute Pasteur in Paris, Strasbourg and Nancy, which is an essential pre-requisite to be successful in their research focus, since locally there is a weakness in immunological expertise" We would like to clarify this point: we developed collaborations with immunologists from other research centers, "since locally there is a weakness in **immune-virological expertise**. This point is important to be stated into the report, because there are locally several immunologist-researchers working on autoimmunity and cancer physiopathology mechanisms.

The BSL3 structure, which is currently under construction, is also an important new infrastructure for our research unit: however, the committee sees a certain weakness in the proposed funding model for the running costs. The day of HCERES evaluation was focused onto the evaluation of the unit scientific production or organization, and not on the detailed scientific project and its financial plan. Only two slides were presented

about the BSL3 project. Further BSL3 maintenance costs will be first supported by URCA as defined in an ongoing official convention in preparation, with planned CardioVir retributions towards URCA that will be related to emerging scientific project grants on emerging viruses as well fundings obtained by analytical services or medical analyses performed (web site services) by the CardioVir team in BSL3 conditions. BSL3 will be an academic as well an official tool for Grand-Est ARS (Agence Régionale de Santé) for the epidemiological survey concerning highly pathogens influenza viruses as well other potential worldwide emerging viruses. Because this BSL3 structure will be academic with a good visibility in the Champagne Ardennes area we plan to develop collaborations with local or industrial partners.

Remarkable Cardiovir papers are related with Enterovirus induced cardiomyopathy mechanisms and all of the major 20 % papers concerns cardiotropic viruses including SARS-Co-V-2 manuscripts as stated into the HCERES Self-Assessment document (SAD).

Yours sincerely

President



Guillaume GELLÉ

Monsieur Thierry COULHON
Président du HCERES

The Hcéres' evaluation reports are available online:
www.hceres.fr

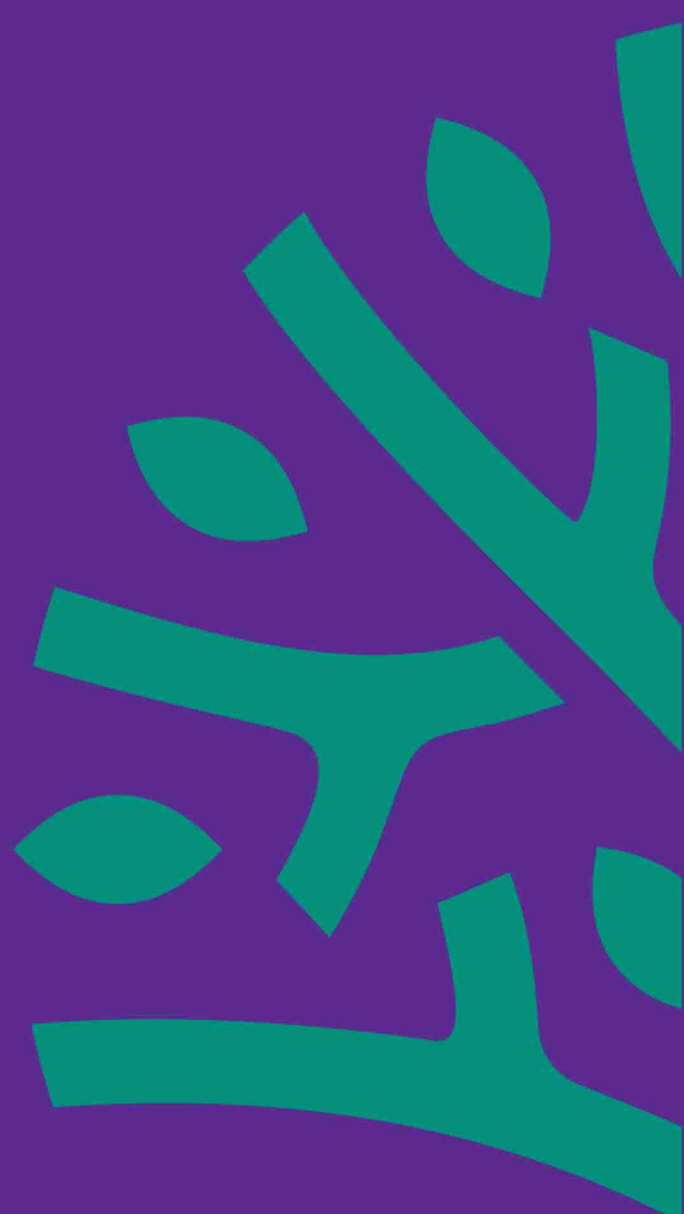
Evaluation of Universities and Schools

Evaluation of research units

Evaluation of the academic formations

Evaluation of the national research organisms

Evaluation and International accreditation



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