Research evaluation

EVALUATION REPORT OF THE UNIT

IVH - Institute for Viral and Liver Diseases

UNDER THE SUPERVISION OF THE FOLLOWING ESTABLISHMENTS AND ORGANISMS:

Université de Strasbourg

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

EVALUATION CAMPAIGN 2022-2023

GROUP C

Report published on June, 29 2023

High Council for evaluation of research and higher education

In the name of the expert committee[1] :

Javier Cubero, 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 Javier Cubero, UCM, Spain
Experts :	Ms Nathalie Callens-Burrea, CNRS, Lille (supporting personnel) Ms Chantal Desdouets, Inserm, Paris Mr Matteo Iannacone, San Raffaele Scientific Institute, Italy Mr Vincent Thibault, CHU Rennes (representative of CNU)

HCÉRES REPRESENTATIVE

Ms Birke Bartosch

CHARACTERISATION OF THE UNIT

- Name: Institute for Viral and Liver Diseases
- Acronym: IVH
- Label and number: UMR S1110
- Composition of the executive team: Head Mr Thomas Baumert, deputy head Mrs Catherine Schuster

SCIENTIFIC PANELS OF THE UNIT

SVE4 Immunité, infection et immunothérapie

SVE7: Prevention, Diagnosis and Treatment of Human Disease
SVE6: Human Physiology and Physiopathology, Ageing

THEMES OF THE UNIT

The main research themes of the unit are ¨Therapeutic discovery and cell circuits of viral and liver diseases¨, ¨Signaling and pathogenesis¨, ¨Molecular Virology¨ of chronic hepatitis B/C/D viruses and ¨Translation of biomarkers and therapeutic approaches into clinical care of liver disease¨. Since 2016, the unit shifted its principal scientific focus from hepatitis viruses to liver disease, focusing on hepatic fibrosis and cancer, addressing the emergence and rapid growth of advanced liver diseases. The unit has established novel technologies to understand virus-host interactions and disease biology on a new level based on functional genomics and system biology approaches, combined with state-of-the-art preclinical models. With its long-standing expertise in virus-host interactions and the discovery of entry inhibitors to prevent and cure the viral infection, the unit developed cutting-edge projects on COVID research.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

The unit is a single team unit located at the medical campus of the University of Strasbourg. It was created on January 1st, 2013, as a continuation of UMR_S748 and then reconducted on January 1st, 2018. The unit is located in a 1 640 m^2 infrastructure at the medical campus of the University of Strasbourg, next to the Service d'hépato-gastroentérologie (Nouvel Hôpital Civil, Strasbourg University Hospital), the Clinical Investigation Center (Inserm CIC 1434), the Institut Hôpital-Universitaire (IHU) Strasbourg and the Centre de Recherche en Biomédecine de Strasbourg (CRBS).

RESEARCH ENVIRONMENT OF THE UNIT

The strategic emplacement of the unit has allowed it to establish strong links with other nearby institutions such as Strasbourg University Hospitals, IHU of Strasbourg, CIC1434, and the CRBS. One of the unit's hallmarks is the joint program with the Strasbourg University Hospitals. Several unit members are involved in the service d'hépato-gastroentérologie, and the DU of UMR S1110 is head of the service. The CIC1434 of the University Hospitals allows for the implementation of phase I and II clinical trials on-site. Joint translational programs with the IHU for Image-Guided Surgery on prevention and treatment of liver cancer have been created. The unit established a new program for the prevention and treatment of liver cancer within the IHU-Strasbourg, which led to the creation of an innovative patient platform for the assessment of liver disease therapeutics and the establishment of an Inserm biobank and to securing major funding awards during the period (ARC TheraHCC 1.0 and 2.0, as well as ANR RHU DELIVER).

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

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	0
Senior scientist (Directeur de recherche, DR) and associate	1
Scientist (Chargé de recherche, CR) and associate	3
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	3

Research supporting personnel (PAR)	16
Subtotal permanent personnel in active employment	**25**
Non-permanent teacher-researchers, researchers and associates	4
Non-permanent research supporting personnel (PAR)	4
Post-docs	4
PhD Students	11
Subtotal non-permanent personnel	**23**
Total	**48**

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

Employer	EC	C	PAR
Inserm	0	4	9
Université de Strasbourg	2	0	6
CHU Strasbourg	0	0	4
Total	**2**	**4**	**19**

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	1 439
Own resources obtained from regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	1 065
Own resources obtained from national calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	11 983
Own resources obtained from international call for projects (total over 6 years of sums obtained)	7 254
Own resources issued from the valorisation, transfer and industrial collaboration (total over 6 years of sums obtained through contracts, patents, service activities, services, etc.)	1 213
Total in euros (k€)	**22 954**

GLOBAL ASSESSMENT

IVH is a mono-unit inserted in the medical campus of the University of Strasbourg in close proximity to the Service d'hépato-gastroenterologie, the Clinical Investigation center, the IHU Strasbourg and the CRBS. The unit comprises (2021) 5 tenured scientists, 8 clinicians, 4 post-docs and 11 PhD students as well as 20 technicians/administrative staff, of which 16 are permanent. The unit is performing state of the art research on liver diseases and therapeutics discovery and has high international visibility. The main aspects pursued by the unit are signalling and pathogenesis, molecular virology, and translation of biomarkers into clinical care. Amongst the major contributions to the field have been: (i) Unravelling cell circuits and interactions driving the progression of liver fibrosis to cancer; (ii) Developing innovative patient-derived models for liver disease and cancer (humanized models); (iii) dissecting viral hepatitis (HBV/HCV/HDV and SARS-COV-2 interactions; and (iv) Translating discoveries (Claudin-1) into novel therapeutic strategies. Another outstanding contribution of the unit has been the description of the human Liver Atlas based on single cell RNA sequencing.

With outstanding support from its supervising institutions, the unit has been highly innovative and productive and is internationally recognized as a centre of excellence. Several top-of-the-notch platforms including cell sorting and imaging systems, and a bioinformatics platform have been created. The work of the unit led to the generation of several original preclinical models and tools to understand and cure liver diseases with a very strong translational focus on the clinical side. In the past 5 years, the unit has obtained ca 20 M€ of external funding from national (RHU, Labex, Idex, ANRS, ANR, Region, etc), European and international sources (ERC, Horizon 2020, NIH), often as coordinator. The unit's scientific output is impressive with 395 articles, of which 91 are original research articles including publications in *New Engl J Med* (2), *Nature* (1), *Nat Commun* (6), *Nat Microbiol* (2), *The Lancet* (1), *The Lancet Oncol* (2), *J Hepatol* (20), *Hepatology* (14), *Gastroenterology* (9) and *Gut* (8). 231 articles were published with unit members as first/last/corresponding authors. The unit has been extremely successful in establishing industrial cooperations, fee-for-service agreements, patents (7 in total, 5 licenced) and created a start-up. Income from the private sector has been 1,2+ M€. Moreover, unit members participate in basic, translational and clinical research promoted by industrial partners for the development of antivirals, and therapeutics against liver fibrosis and cancer using preclinical models.

Finally, the unit has local collaborations with leading institutions such as Strasbourg University Hospitals, IHU Strasbourg, the CIC, the IGBMC, the IBMC and the Institute of Chemistry (UMR 7177) and also built collaborations and networks with leading international experts in the field (MIT, Standford, Harvard, etc). The fact that the unit has attracted an impressive number of international fellows and postgraduate students underlines its international visibility. The unit is offering a supportive environment for the professional development of its students and fellows, either in the academia or in the industry, and is promoting the next generation of young scientists in the Hepatology field.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommendation 1: *The logistics to establish relevant cohorts and tap into clinical material from biobanks is in progress and the unit should build on the availability of such samples to validate findings from in vitro studies:* As recommended the unit obtained the authorization to create its own collection of liver tissue, blood and biopsies; The unit assembled 4 different biobanks through collaborations at local level to validate in vitro observations (Patient Liver Biobank, Patient Liver Cell Biobank, Patient Serum Biobank, Patient PBMC Biobank).

Recommendation 2: *Replace any key members of staff to maintain their competitiveness of the unit.* The unit successfully recruited (a) 2 tenured scientists, (b) 2 expert senior post-doctoral fellows (1 bio-informatician for the computational analysis program and 1 for the patient-derived models' platform, (c) 3 technical staff with expertise in cell biology, virology, model care.

Recommendation 3: *It is essential that the BSL3 is adequately maintained and developed to meet the standards required.* With support of the institutions, the unit successfully renovated the structure to enable expansion of the unit and obtain new space within the old building, replaced vital equipment in the BSL3 (hoods, incubators), acquired a SONY cell sorter for the BSL3 laboratory and obtained additional funding for A3 equipment. One limitation remaining is certainly the lack of personnel dedicated to the A3 facilities.

Recommendation 4: *Address the challenges faced with developing the current environment and ensure that it can attract top-class scientific staff and students to achieve its goals.* As recommended, the unit consolidated and expanded scientific programs of excellence (Liver disease and liver cancer, viruses, disease biology and cancer, emerging viruses SARS-CoV-2), obtained competitive research funding (2 ERC-AdG, 2 ERC- PoC, 4 NIH, 1 RHU, 1 ANR JCJC, 14 ANRS), which allowed the recruitment of high-level post docs (21) and Ph.D. students (28). Moreover, the unit promoted and extended translational research programs, (IHU, TheraHCC, RHU) and extended training of MD-Ph.D. students to physician scientists (Labex, Graduate School EUR IMCBio). In addition, the unit successfully promoted tech transfer (drug discovery and development in collaboration with industry), created the biotech startup Alentis and has a strong IP portfolio (7 patents).

B - EVALUATION AREAS

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

Assessment on the unit's resources

The unit has outstanding resources and exceptional grant leverage with peer-reviewed funding of 23 M€.

Assessment on the scientific objectives of the unit

The unit has set itself objectives highly relevant for liver diseases and beyond, and is highly competitive in the Hepatology field.

Assessment on the functioning of the unit

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

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

Strengths and possibilities linked to the context

The unit, is a single team unit located at the medical campus of the University of Strasbourg. It is located in a 1 640 m^2 infrastructure at the medical campus of the University of Strasbourg, next to the *Service d'hépato-gastroentérologie* (*Nouvel Hôpital Civil,* Strasbourg University Hospital), the Clinical Investigation Center (Inserm CIC 1434), the *Institut Hospitalo-Universitaire* (IHU) Strasbourg and the *Centre de Recherche en Biomédecine de Strasbourg* (CRBS). This state-of-the-art environment ensures that the unit's fundamental, translational and clinical research program is executed with the highest quality and efficiency.

The unit is composed of an international multi-disciplinary team of molecular and cell biologists, virologists, preclinical model experts, bioinformaticians, clinical hepatologists, and surgeons. The staff includes highly qualified faculty members, senior and junior scientists, clinicians, surgeons, engineers, assistant engineers, technicians, and administrative personnel with 25 positions being permanent/tenured, and 23 positions, including Ph.D. students, postdocs, engineers, and technicians, being funded by external grants.

The unit has created a highly competitive scientific, training, and technology-transfer program, and is a Laboratory of Excellence since 2011. The unit has carried out several prestigious international, European, and national programs and also received donations from charities and funding from local, national and private sources. In total, the unit benefited from peer-reviewed funding of 23 M€. This funding has allowed creating networks of excellence with other international leaders in the field as well as the funding of Ph.D. and postdoc fellowships. Moreover, the unit's activities are regularly supported by annual allocations of its supervisory institutions (Inserm and University of Strasbourg), which cover running costs, equipment purchases – including a Zeiss microscope with a fluidic system, the SH800S Cell Sorter, and the Vevo 3100 micro-ultrasound imaging system FUJIFILM VisualSonics -, and building maintenance costs. In summary, the total internal funding 2016-2021 for running costs, equipment, and maintenance was 1,7+ M€.

Notably, the unit is structured as a single team where financial, human resources are shared among the different research projects, and where each group leader contributes with their grants to the unit's mutualized budget. The unit's infrastructure includes several laboratories of molecular and cell biology, one confinement BSL3 laboratory, and all major equipment mentioned earlier as well as computational equipment. This state-of-the-art environment ensures that the unit's program is executed with high quality and efficiency.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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 research program combines basic, translational, and clinical investigation resulting in high-impact discoveries translated into the clinic. One of the main lines of research is advanced liver fibrosis, a significant public health burden with rising prevalence with an unmet medical need for novel anti-fibrotic therapies. Scientific aims of the unit include the unravelling of cell circuits driving liver disease progression, the development of innovative patient-derived models for liver disease, the characterization of HBV / HCV /HDV/ SARS-CoV-2 - hepatocyte interactions and the translation of discoveries into novel therapeutic strategies.

Undoubtedly, the unit has built excellence, training and innovation with strong international collaborations. The unit is a powerhouse of scientific excellence, training, and innovation. Due to its strategic location within the fantastic Strasbourg ecosystem, a cornerstone of the unit's success is its strong integration within the Strasbourg competitiveness cluster. This unique pole of excellence includes leading institutions such as Strasbourg University Hospitals, IHU Strasbourg, the Center for Clinical Investigations (CIC), the *Institut de Génétique et de Biologie Moléculaire et Cellulaire* (IGBMC) the *Institut de Biologie Moléculaire et Cellulaire* (IBMC), and the *Institut de Chimie* (UMR 7177).

The close collaborations and the long-standing established partnership with these cutting-edge institutes have led to significant discoveries with the concrete potential to improve patient outcomes. Besides the local ecosystem, the unit has built collaborations and networks with leading international experts in the field, including networks for systems biology and computational analyses at the Broad Institute of MIT and Harvard, UTSW Dallas, Hiroshima U, Tokyo U, Oxford U, DKFZ Heidelberg, HZI Hannover and other networks with leading international experts in the field.
Currently, the unit is leading an ARC-funded joint program on liver cancer in close collaboration with the Hospital University Institute for Image-Guided Surgery (IHU Strasbourg). From 2022, the institute will lead the prestigious RHU ANR program "DELIVER", a cutting-edge public-private R&D program that will combine patient-derived models and integrate the latest imaging technologies with AI and large prospective cohorts of patients included in HCC surveillance programs to deliver therapeutic innovation for advanced liver fibrosis and HCC. The ERC-AdG-FIBCAN will be launched in July 2022 and will focus on novel therapeutic approaches to treat and prevent advanced liver fibrosis and liver cancer, using innovative patient-derived models. In addition, the unit is actively participating and shaping the initiative of excellence of the University of Strasbourg as a laureate of a Laboratory of Excellence and several Initiative d'excellence (Idex) awards of the University Strasbourg. Over 50 randomized clinical trials for the evaluation of HBV and HCV antivirals as well as liver cancer therapies were executed within the frame of the UMR_S1110 translational program at Strasbourg University Hospitals clinical services and the CIC (sponsored by Gilead, Transgene, BMS, Roche, and others). For commercialization, networks within the regional Pharma hub in Basel and Paris (Roche, Novartis, Sanofi, Guerbet), the tri-national Biovalley, and the Swiss and French start-up incubators BaseLaunch and Semia. Finally, thanks to a close collaboration with *Fondation Unistra*, the unit designed a dissemination and valorization strategy, including fundraising, media coverage, press releases, flyers, posters, and brochures, to promote its discoveries and to raise awareness among patients affected by chronic liver diseases.

Importantly, the steering committee of the unit is in charge of decisions about policy on research and exploitation of research findings. Collectively, it promotes an approach of co-authorship aiming to valorize all the scientists, engineers, and technicians who made significant scientific contributions to the manuscripts, sharing responsibility and accountability for the unit's results.

According to the same principles, intellectual property and patents' inventorship are carefully evaluated to promote and valorize scientists who made an intellectual contribution, solely or jointly, to at least one element of a claim in a patent.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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

Since its beginning, the unit has been practicing a policy of equality and non-discrimination in the hiring selection process, promoting gender equality and diversity with more than 10 nationalities represented in the unit over the period (e.g., Lebanon, Belgium, Italy, Spain, Portugal, Algeria, India, China, Germany, Australia, Tunisia, Canada, Bolivia, USA). Recruitments are performed by a mixed jury, composed of senior scientists and post-docs, following a several-step screening procedure to prioritize key skills, the use of neutral language for job descriptions, training within the organization with a continuous development and involving more people in the interview process. Whereas selection of candidates is based on their quality over a forced gender-balanced composition, the representation of women in decision-making positions does not present a balanced ratio. However, the unit is working actively to identify top-level female applicants and try and reduce the gender gap in senior decision-making positions.
All unit members have an allocated bench space (for individuals performing wet lab work), an allocated desk area, and a personal computer. Training and safety are implemented for all workers.
For data management the unit has a 30 TB state-of-the-art server infrastructure doted with operational security, managed nationally by Inserm DSI teams, and a platform for messaging (Unistra). A recovery plan is also well established and the electronic lab notebook project is running.
The unit is fully committed to environmental preservation and sustainable development by encouraging staff, students, and postdocs to work from home whenever feasible except for maintenance of important facilities (BLS3, building, labs) and the enforcement of postCOVID measurements and testing.

Weaknesses and risks linked to the context

Women at senior level are currently underrepresented in the unit.
The number of technical and administrative staff seem to be insufficient, and this situation is a concerning risk for the future of the unit.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The attractiveness of the unit is outstanding at the national and international levels.

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

During the reported period, unit members have participated in more than 120 international and national conferences (EASL, AASLD, ILCA, annual HBV and HCV meetings, ALSD, ANRS). Unit scientists presented their work at international and national events as oral communications and poster presentations and gave 45 talks as invited speakers (EASL, HBV, and HCV meeting, EESCV congress, CASL).

Unit members actively participate and contribute to the larger community at the local, national, and international levels. Senior researchers were actively involved in international conferences (French-Swiss-German Gastroenterology Regio-meeting, Global Hepatitis Summit, EASL Basic Research Symposium, EASL Workshop "Liver circadian clock", Journées Francophones de Virologie).
The unit's scientists and group leaders, are regularly involved in editorial activities in internationally recognized journals in the field. The head of unit is associate editor of the *Journal of Hepatology*, the most prestigious journal in liver disease. He is also a member of the editorial board of the high-profile journals *Gastroenterology, Hepatology*, and *Hepatology International*.

Finally, members of the unit take part in research steering or scientific expertise bodies at international, European and national levels (ANRS, Deutsche Leberstiftung, Eurolife, Inserm, SGBM, Innasco, Hepatitis B Foundation, etc).

In November 2017, the unit´s leader became a Senior Member of the Institut Universitaire de France (IUF) for his achievements on prevention and treatment of liver disease and liver cancer, development of a vaccine against the hepatitis C virus, and studies on cellular factors for the cure of chronic hepatitis B.
In April 2021, he was also elected as foreign member of the American Association of Physicians (AAP).

The unit co-leader is the Head of the Doctoral School for Life Sciences and Health since 2018, Référente Scientifique Inserm Région Grand-Est since 2019 and Présidente CSS5.
Inserm since 2022.

Over the period 2016-2021, unit members received several prestigious awards including Prix "*Mémain Pelletier" de l'Académie des Sciences*, Eurolife distinguished lecture, *Prix de thèse de la Fondation de l'Université de Strasbourg* and *Prix de thèse de la Société de Biologie de Strasbourg*, Best poster prize HBV meeting, Best poster prize ILC, *Prix de thèse de la Société de Biologie de Strasbourg*, *Prix de thèse de la commission recherche de l'Université de Strasbourg*, Prix de thèse ANRS, *Prix de thèse "Albert Schweitzer" par le Chapitre Saint Thomas*.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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

Strengths and possibilities linked to the context

The unit provides exceptional training and mentoring of undergraduate and graduate students, post-docs, scientists, and medical doctors. During the reporting period, the unit trained 28 Ph.D. students and 9 Ph. D.s for MD in translational medicine. Ph.D. students are paired up with postdocs, senior staff, or senior level Ph.D. students to accelerate training, to facilitate exchange of technical expertise, and to help them grow and flourish while simultaneously accelerating the research programs. This experience is mutually beneficial since the more senior staff members also have the opportunity to supervise students and manage projects in close association with the group leader, thus preparing them for their future roles as independent researchers. Numerous Ph.D. awards show the quality of the students throughout the evaluation period; they participate on average in the publication of 6 papers overall, with 1.5 first author experimental work publications per student in top-level journals. Ph.D. students are encouraged to participate in publication and review writing to prepare them for their future role as researchers. Further training for Ph.D. students is provided by a summer and winter school hosted by the Doctoral School of Life and Health Sciences in Strasbourg. Moreover, Ph.D. students attend major national and international scientific meetings to present their work (average of 5 communications per Ph.D. student within their Ph.D. training period).
During the reporting period, the unit has attracted and trained 21 postdocs. The post-doctoral fellows are world-wide recruited. Senior staff members regularly have individual meetings with postdocs (at least one meeting per week) to discuss aspects of their ongoing tasks, future directions, timelines, and deliverables to ensure smooth progression of projects while providing guidance and support. To qualify post docs for their future roles as researchers, all the postdocs are encouraged to prepare grant applications, apply for fellowships, travel grants and awards, and participate in review writing. Ph.D. students and post docs mentored by the unit have obtained excellent academic research or industry positions worldwide.
Additionally, the unit hosts every year medical students to introduce them to "bench to bedside" translational research. During the reporting period, the unit mentored 9 medical doctors pursuing a Ph.D., providing the next generation of leaders in liver disease in clinical medicine and research. To foster the interdisciplinary state-of-the-art training in translational research of medical students and doctors, the unit organizes meetings gathering clinicians, surgeons, scientists, and imaging medical experts. Additionally, the unit organizes a monthly staff meeting, and a bi-weekly work-in-progress meeting.
Several unit alumni have received tenured positions in French governmental research organizations and faculty positions outside France.
Additionally, integrity is the pillar of the unit´s high-quality research, and it is fostered through training in best practices. Research integrity training offers are regularly communicated to unit members. All staff members attend periodically training sessions to acquire knowledge and skills to ensure scientific integrity (eg: responsibilities in collective research work, data reliability and traceability, lab notebook, open science).

Weaknesses and risks linked to the context

The extensive workload and involvement of PIs in additional tasks and projects may impact the quality of mentoring of PhD and postdocs.
Although young PIs benefit from an excellent scientific environment, their emergence as independent leaders is difficult due to the structuration of the team into a single unit.

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 unit was awarded seven European grants ((ERC-AdG2), ERC-PoC(2), H2020(2), HORIZON EU(1)) totaling 5,4 M€, as well as 5 international projects (NIH NIAID (2), US Department of Defense (1), NIH NCI (1), NIH NIDDK (1)) for a total of 1,4 M€.

The unit is involved in several initiatives of the Investments for the Future program (PIA): Since 2011, the unit has been a laureate of the French government's highly competitive and prestigious Laboratory of Excellence Award (Labex). An excellent evaluation of the Labex in 2015 by an international review committee, allows the unit to support long-term funding of high-risk, high-impact projects. Since 2021, as Labex HepSYS, the unit is part of the Institut Thématique Interdisciplinaire IMCBio+/ITI IMCBio+, created by the University of Strasbourg in the frame of the Idex. During the period 2016-2019, the unit secured 2,9 M€ (Labex HepSYS 2,489 k€, Idex 420 k€). In 2021, the unit was awarded an RHU totaling 6,7 M€, the only one in the Grand Est Region of France. The RHU DELIVER is coordinated by the unit. With a unit budget of 4,1 M€, DELIVER focuses on therapeutic innovation for advanced liver diseases and cancer. Overall, the unit has built strong collaborations and partnerships with local institutions which are part of PIA initiatives: IHU Strasbourg, SATT Conectus, INFRA Phenomin.

The unit has secured three awards that they led amounting to 591 k€ from the National Research Agency (ANR) during the reporting period (TargEnt, Terminanion, DELTArget (ANR JCJC)). 14 programs have been funded by the ANRS. Furthermore, funding from l'Institut National du Cancer (INCa) and local authorities (Region Grand-Est, Cancéropole Grand-Est, Association contre le cancer) has been obtained.

The high quality of the unit's cutting-edge research program is highlighted by the numerous prestigious awards and funding received in international, European, and national competitive calls for projects, for a total of 20,3 M€. This impressive funding success has created the leverage to fund Ph.D. and post-doctoral fellowships, as well as the recruitment of engineers and technicians. Over the period 2016-2021, the unit has created the leverage to fund 49 fellowships (Ph.D. and postdoctoral) and to recruit 15 engineers and technicians, for a total of 2,76 M€.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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

Strengths and possibilities linked to the context

The unit's BSL3 laboratory offers a safe and contained environment for the production and manipulation of viruses such as HCV, HBV, HDV and SARS-CoV-2. The state-of-the-art patient-derived liver spheroid platform generates and supplies cutting-edge patient-derived models for high-quality translational research. Moreover, the bioinformatics platform models cell circuits in human disease biology. The unit's expertise comprises the integration of cell, preclinical model, and patient data contributing to unravelling novel therapeutic concepts and targets, single-cell transcriptomics and proteomics, as well as data analyses from epigenetic (ChIP-seq), mutational (DNA-seq), and transcriptomic (RNA-seq) next-generation sequencing. Functional gene pathway enrichment analysis and drug screen assessment using genome-wide and signature approaches (such as NanoString technology) are being performed. Furthermore, this unit has a state-of-the-artpreclinical model facility , where maintenance, safety and training are implemented. External users are welcome and facilities, infrastructures, and approaches are available to the scientific community within collaborations or fee-for-service agreements.
The unit qualified for BEI resources registration in respect to their work programme on SARS CoV 2. BEI resources, established by the NIAID, provides reagents, tools and information for priority pathogens and emerging infectious disease agents.
Cleaning procedures, protective equipment and emergency stations are installed in all facilities. Technicians are highly trained, manage platforms, major equipment and organize demonstrations. The unit offers its services to external users.

Weaknesses and risks linked to the context

Workload of some technical and administrative staff is too large considering the available manpower. This lack of staff may eventually jeopardize the outstanding productivity of the entire unit.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The overall scientific production of the unit is outstanding with an average production of 79 publications per year and a total of 213 publications with unit members as first-last-corresponding authors.

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

Strengths and possibilities linked to the context

Over 2016-2021 unit scientists have published 395 peer-reviewed articles with (91) original, (139) review articles, and (165) clinical articles, and the unit's publications have received more than 5 000 citations. Articles were published in high-profile journals such as *New Engl J Med* (2), *Nature* (1), *Nat Commun* (6), *Nat Microbiol* (2), *The Lancet* (1), *The Lancet Oncol* (2), *J Hepatol* (20), *Hepatology* (14), *Gastroenterology* (9), *Gut* (8). More than 70% of the unit's articles have been published in the best and more visible journals of their disciplines. The high-level science of the unit is further highlighted by the international and national collaborations resulting in several co-publications in the most prestigious journals. Amongst the unit's publications, 213 were published as a first-last-corresponding author in the most prominent journals in infectious disease, virology, molecular biology, cell biology, hepatology, gastroenterology, cancer research, immunology, drug development, genetics, medicine, and surgery.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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

On average, the unit has published (79) papers per year, including original and clinical peer-reviewed publications, and peer-reviewed reviews and editorials. Overall, more than 70% of the unit's production has been published in journals the best journals of their disciplines, and 1,5 papers as average per Ph.D. student. In line with the unit's scientific strategy, all professors and group leaders contribute to the scientific production of the unit as lead- or co-authors. According to the unit's publication policy, Ph.D. students and post-docs are regularly included as lead- or co-authors pending their research work contributions; over the past five years, their participation has represented 30% of the unit's total publications. During the reporting period, Ph.D. students contributed to the publication of 130/395 articles, 38 of which as first authors. Post-doctoral fellows have contributed to the publication of 105/395 articles, 25 of which as first authors.

Weaknesses and risks linked to the context

Not all articles are yet open access due to missing administrative staff, necessary to submit and upload all the documents. The lack of administrative personnel could eventually lead to less visibility of the team despite its outstanding productivity.

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 promotes and spreads a culture of scientific integrity by supervising and training students to perform critical analysis of scientific data, prevent plagiarism and by informing students about legal and regulatory texts and ethical rules, especially those concerning human, and environmental research. An electronic laboratory notebook is compulsory for all unit members, where raw data and conditions of original experiments are accurately recorded so they can be reproduced.

In 2020, the unit created the collection LivMOD (RIPH2 LivMod IDRCB 2019-A00738-49) to establish translational pre-clinical models for the study of tumors and chronic liver diseases. This protocol allows obtaining human liver tissues, blood, and biopsies, from liver disease patients undergoing liver resection with informed consent from all patients for anonymity.
The unit has the lawful basis for data processing and applies the 3R rule. Finally, to promote open science, the unit is committed to exploiting multidisciplinary repository platforms and publishes in open-access journals.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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 outstanding as exemplified by 15 industrial contracts, 7 patents, of which 5 are commercialized, and creation of start-up companies.

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

Strengths and possibilities linked to the context

Several foundations have supported the unit's research programs including the *Fondation Recherche Médicale* FRM and Fondations ARC and Unistra. Unit members participate in basic, translational, and clinical research promoted by industrial partners including Biotest, Aligos, Genovac, Roche, Gilead, Indus, Virtexx. On behalf of unit, SATT Conectus, which handles the IP management of the unit, has established fee-for-service agreements with Janssen, Biotest and Indus to develop antivirals in preclinical models. Additional collaborative research agreements have been implemented (Sanofi, InnaVirax, Kyowa Hakko Kirin, Aligos, Addgene, Inoviem Scientific, RiverStone).

The unit has implemented a solid and effective strategy to promote and accelerate the technology transfer process. The unit's project managers are trained to seize the most attractive funding opportunities to support the innovation process by regularly participating in EU training sessions and systematically interacting with local actors (Region Grand Est, SATT Conectus, BPI France). In 2021, the unit evaluatedthe participation in the calls: EIC Pathfinder and transition.

Weaknesses and risks linked to the context

All non-academic activities solely rely on the unit leader. Extension of non-academic activities to several other members of the team would ensure its durability and strengthening.

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

Strengths and possibilities linked to the context

The unit has obtained 7 patents of which 5 have been commercialized, created a start-up (Alentis Therapeutics Basel, Alentis Development Strasbourg), performed 10 clinical trials and obtained 15 industry contracts (University of Alberta, Sanovi Aventis, Sanofi, Riverstone, Meletios Therapeutics, Kyowa Hakko Kirin, Janssen, Aligos Therapeutics, Alentis) over the reporting period. In total, 1+ M€ collaborative and fee-for-service revenues have been collected by the unit.
The Alentis Therapeutics start-up, based on the units ground-breaking research, was created in 2018 with the units head as founder and supported by 121 000 € seed funding from BaseLaunch (Basel incubator in Switzerland). In 2019, a french spin-off, Alentis Development, was created in Strasbourg.
Therefore, and as mentioned earlier, the strong implication of the unit with non-academic partners is highlighted by the regular participation of unit members in basic, translational, and clinical research promoted by industrial partners.

Weaknesses and risks linked to the context

No weaknesses to be reported.

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

Strengths and possibilities linked to the context

Unit scientists are actively participating at events for the general public including debates on science and society such as '*Visioconférence Grand Public COVID-19 et Vaccination – Société de Biologie de Strasbourg*', '*Des artistes au cabinet du président?*', '*Histoire d'en parler: la vaccination de l'antiquité à nos jours*' and local interventions at the French Festival of Science. The work of the unit is regularly covered in regional, national and international journals. The unit communicates actively on LinkedIn, Twitter and on its website.
In addition, the unit regularly participated in disseminating knowledge to patient associations such as SOS Hépatites Alsace and SELVHA, the expert medical network in Alsace for viral hepatitis.

Moreover, the unit established a well-defined strategy for outreach activities to get relevant exposure and make the fruit of the unit's work broadly available via press releases, its website, social media and informative videos. Notably, during the reporting period, unit scientists have taken part in different initiatives to raise awareness amongst high school and young students.

Weaknesses and risks linked to the context

There is no budget for the involvement of technical staff in the public events and science dissemination.

C - RECOMMENDATIONS TO THE UNIT

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

The unit should pursue the recruitment of women for a junior professorship as well as for senior positions to implement gender balance within the unit.
The unit should increase the number of BSL3 in vivo facility and administrative staff, and replace retiring staff members.
The unit should ensure that they have enough administrative staff to make open access possible.
Communication concerning the management of psychosocial risks among the members of the unit should be promoted.
The unit should resume all social activities as before the COVID19 crisis.
It is recommended that all staff members and, particularly, members working at BLS3 and A3 have a follow-up by the Preventive Medicine Department.

Recommendations regarding the Evaluation Area 2: Attractiveness

PhD mentoring should be individualized to avoid supervision of students by several PIs.
Continuous discussion between the unit leaders and the young PIs is recommended for the mutual benefit and progress of the unit, in terms of emergence.

Recommendations regarding Evaluation Area 3: Scientific Production

We recommend the unit to continue their outstanding scientific production.

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

The unit should have a budget for activities concerning the dissemination of science, specifically for technical staff.
The unit is encouraged to promote communications via social networks.
Young PIs are encouraged to reinforce links with industry.

CONDUCT OF THE INTERVIEWS

Date

Start: 24 October 2022 at 8:30

End: 24 October 2022 at 18:30

Interview conducted: online

INTERVIEW SCHEDULE

8:30-9:00	**Hcéres Committee meeting** *(closed-door meeting)*
9:00-9:05	**Hcéres Rules and procedures by B. Bartosch** *(all unit members)*
9:05-10:00	**Administrative & Scientific presentations of the Unit by Prof. T. Baumert** (55min) **Overall Presentation of the Unit** **Highlights and Projects: Next challenges** *(all unit members)*
10:00-10:30	**Discussion** *(all unit members)*
10:30-10:50	**Debriefing of committee and break** *(closed door meeting)*
10:50-11:30	**Meeting with ITAs (in French)** *In the absence of any managing staff*
11:30-11:50	**Meeting with researchers** *In the absence of any managing staff*
11:50-12:10	**Meeting with post-docs and students** *In the absence of any managing staff*
12:10-13:30	**Lunch Break**
13:30-14:15	**Meeting with institution representatives: Inserm/University of Strasbourg** *(closed door meeting)*
14:15-15:00	**Debriefing of committee** *(closed door meeting)*
15:00-15:20	**Meeting with the Management Team of the Unit** *(closed door meeting)*
15:20-15:30	**Break**
15:30-18:30	**Redaction of the final report** *(closed door meeting)*
18:30	**End of the visit**

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 8 juin 2023

Objet : Rapport DER-PUR230023204 - IVH - Institut de recherche sur les maladies virales et hépatiques

Réf. : RB/FF/ 2023-372

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

Cher Collègue,

Affaire suivie par :
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Responsable du département Administration de la recherche et accompagnement des chercheurs
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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 « Institut de recherche sur les maladies virales et hépatiques » (IVH – UMR_S 1110).

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

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

Rémi Barillon

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