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*19 February 2019*

# Evaluation of LIH-DII

## Report by the external peer review committee

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Rudi Beyaert (chair)
Seppo Meri
Ronald van Ree
Janna van Belle, Anke Nooijen (rapporteurs)

# Executive summary

This report presents the results of the peer review of the Department of Infection and Immunity (DII) of the Luxembourg Institute of Health (LIH). The review covers the period 2014-2017 and considers research strategy and quality, scientific and societal impact, and the management and governance.

The audit was performed by an independent external assessment committee, consisting of three internationally renowned researchers in the field of the research of the Department, prof. Rudi Beyaert (chair), prof. Seppo Meri and prof. Ronald van Ree. Janna van Belle and Anke Nooijen (Technopolis Group, The Netherlands) organized the evaluation, moderated the hearings, and supported the committee in their report.

The committee would like to thank everyone involved in preparing and implementing the hearing at the LIH-DII, for making the documentation available, and for participating in interviews, which were very open-minded.

The report discusses the expert team's observations gathered during the evaluation process. In general, the committee is impressed by the dynamic development and the performance of the department, which is still very young. During the evaluation period the research unit underwent several structural changes that were accompanied by significant reorganizations and strategy allignments. The experts rate the overall standard of the facilities as very high. The director has to be praised for providing strong leadership and taking into account the recommendations of the previous evaluation panel very seriously. As a consequence, the department has already begun to acquire higher visibility, both within LIH and at the national and international level. The expert panel was impressed by the showcased examples of research, which covered a broad range of subjects. The PIs should be commended for doing top fundamenteal research addressing problems of clinical relevance and for providing excellent services to the public or scientific community. The expert team also had a positive overall impression of the students and postdocs and their training opportunities. Together, these achievements provide a firm foundation upon which to build the future. The main challenges for the LIH-DII are (1) to bring more focus in the different research themes and to enhance synergy between groups in order to increase visibility at the international scene; (2) to build bridges to the clinic, while finding a good equilibrium between basic research, clinical research, and public health services; (3) to improve internal communication on LIH-DII's new mission, funding policies and evaluation criteria; (4) to strengthen its international position by acquiring competitive research funding from European grants as well as from research contracts with the private sector. At the end of the report, the committee provides several recommendations for further development of existing strengths and overcoming observed weaknesses.

The current budget of LIH-DII is in line with the importance and relevance of the research being achieved and its societal impact. However, turning the fundamental findings of the LIH-DII into medical opportunities and successfully integrating the LIH-DII in LIH's new mission will not only require the continuous financial support from the block grant, but also a clear plan from LIH to provide LIH-DII with better support in terms of administration and communication, easy accessible research infrastructure and core services, and a clear plan to integrate its activities in a well-defined strategic plan at national level, within LIH and with the medical sector.

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# 1 Introduction

## 1.1 Background

This report presents the results of the peer review of the Department of Infection and Immunity (DII) of the Luxembourg Institute of Health (LIH). LIH has the mission to deliver scientific, economic and societal value for Luxembourg by performing research, studies and developments in the fields of clinically-oriented biomedical research and public health. LIH's activities lead to the generation of new knowledge in disease mechanisms, epidemiology, diagnostics and treatments of human diseases, and the improved understanding of health determinants and of the financial structures of health care. LIH-DII arose from a merger between the Laboratory of Retrovirology (LRTV) and the Laboratory of Immunogenetics and Allergology (LIGA) in 2014. In 2015 the Department of Immunology (LNSI) was integrated into LIH-DII. Since then LIH-DII's mission was 'to induce immune tolerance and activate the immune system for human health, thereby translating basic science into clinical practice for improved health care' (source: LIH-DII's self-assessment report).

The peer review is part of an evaluation of the three research institutes under the responsibility of the Luxembourg Ministry of Education, Science and Research (MESR). The evaluations cover the period 2014-2017 and consider scientific performance, relevance for society including client and partner interaction and the governance and organisation as requirement to sustain the ability and suitability for promoting both scientific performance and interaction with clients. The evaluation has been assigned to Technopolis Group (www.technopolis-group.com).

The results of this peer review feed into the evaluation of LIH as an institute and into the evaluation of the three institutes at national level. For this reason, the chairman of the LIH-DII peer review also participates in the peer review of LIH at institutional level. The results are intended for MESR to (re)define their relation to the institute; for the institutes to help them to improve their performance further and for other (mainly public) stakeholders to use as they find suitable.

The peer review set-up has been designed by Technopolis Group, based on the Terms of reference from MESR. It aligns with good practices used in many evaluations.

## 1.2 Composition of the Committee, independence, data provided and procedures followed

### *1.2.1 Composition of the Committee*

The audit was performed by an independent external assessment committee, consisting of three internationally renowned researchers in the field of the research of the department:

- Chairman: Rudi Beyaert (VIB-UGent Center for Inflammation Research, Ghent, Belgium)
- Seppo Meri (Department of Bacteriology and Immunology, University of Helsinki, Finland)
- Ronald van Ree (Amsterdam Medical Centre AMC)

Short CV's from all assessment committee members are attached in Appendix A.

Janna van Belle and Anke Nooijen (Technopolis Group, The Netherlands) acted as support for the peer review committee.

### *1.2.2 Independence*

Any existing personal or professional relationships between committee members and programmes under review were reported and discussed in the committee meeting to safeguard an independent assessment of the quality of LIH-DII and its research programmes in an unbiased and independent way. The Committee concluded that there were no close relations or dependencies and that there was no risk in terms of bias or undue influence.

### *1.2.3 Data provided to the Committee*

In preparation of the review the peers received the following information:

- A self-assessment report of LIH at institute level
- A self-assessment report of LIH-DII at department level
- A background report for the peer review of LIH prepared by Technopolis Group, including a.o. an analysis of the participation of LIH in FNR and EC research projects and a bibliometric analysis of the publications of LIH (by ECOOM).

The assessment in combination with the discussions of the peer review committee with the research leaders, researchers and stakeholders allowed an objective evaluation of LIH-DII.

### *1.2.4 Procedures followed by the Committee*

The final assessments are based on the documentation provided by the Institute, the key publications and the site visit to LIH-DII in Luxembourg on 18-19 September 2018 (programme in Appendix B).

At the beginning of the site visit, the Committee was briefed by Robert Kerger of MESR and Janna van Belle and Anke Nooijen of Technopolis Group about the objectives of the evaluation in general and of the evaluation by the committee in particular. During this meeting, several questions were clarified. The Committee also agreed upon procedural matters and aspects of the assessment.

At the end of the site visit and interviews the Committee discussed the conclusions and recommendations. Preliminary draft conclusions were presented to the participants in the discussions including the management of LIH-DII and LIH and to the representatives of MESR and the Ministry of Health.

The first version of this report was drafted by the peers within a week after the site visit to Luxemburg. The report was finalised through email exchanges. The consolidated version was presented to the Institute beginning-October 2018. The reaction of LIH-DII was discussed by email by the Committee and led to adjustments of some factual points. The final report was then submitted to MESR.

For the assessment of the quality of the research, LIH-DII was compared at the international level with their peers. Publication and citation records were examined; major achievements were considered and the capacity to be competitive in international funding and in attracting highly qualified students and collaborators was discussed. For obtaining a view of the relevance for science, elements such as recognition as a knowledge centre, participation in expert groups, leadership in EU projects, membership on editorial boards and professional societies were employed.

The relevance of LIH-DII in relation to health research was judged at the international and national level. Services and expertise rendered to private and public clients and partners and the impact on the general public served to assess the relevance for society.

The aspects of governance and organisation of LIH-DII were mainly focused on the discussion about the strategy with LIH-DII staff members. The findings are presented in this report. The findings related to the departmental organisation show adequate robustness, since they have been discussed with the most relevant stakeholders. The findings related to the positioning of the department within LIH and the positioning of LIH in the health (research and education) landscape in Luxembourg and in international perspective give the reflection of the peers on the vision of LIH-DII but require further input from other stakeholders inside and outside LIH. Therefore, these findings are preliminary and will feed into the evaluation of LIH at institute level.

It has to be noted that the budget- and financial management of LIH-DII and its coherence with its missions and scientific program have not been evaluated in detail. This is due to the fact that there was not sufficiently precise and specific information made available to the Committee neither in the self-assessment report, nor in the background report prepared by Technopolis Group, nor during the site-review.

# 2 The positioning of DII research: rationale and strategy

## 2.1 DII strategy and targets

**Mission.** As a goal, by the end of the year 2021, LIH-DII has the aim to be recognized as a global leader in research and innovation on immune-mediated diseases, immune-aging, neuro-inflammation and cancer immunology. Based on its research excellence, the LIH-DII will also strengthen its activities as a premier service provider and national focal point for preparedness and surveillance in infectious diseases for several governmental (e.g., Luxembourg Ministry of Health, Ministry of Agriculture, Ministry of Foreign Affairs) and non-governmental agencies (e.g., World Health Organisation (WHO), Laos- Lux-Pasteur Institute) over the next 4 years.

During the years 2014-2017, the period under review, the research unit underwent several structural changes that were accompanied by significant reorganizations and strategy alignments, according to the following mission statement: 'Inducing Immune Tolerance and Activating the Immune System for Human Health – Translating Basic Science into Clinical Practice for Improved Health Care, by investigating the following disease areas: a) Non-communicable diseases (NCD), b) Tumor immunology, c) Infectious diseases/virology, d) Immunotherapy and vaccination research as the synthesis between NCD, cancer and infectious diseases. Since 2017 LIH's new mission is **"to impact on patients by performing and translating excellent biomedical research"**. This will also have a major impact on the development of LIH-DII's mission, implicating a stronger focus on translation. Because of the clinical nature of LIH-DII's research themes, there will be a need for closer collaboration with partners, who take care of patients and handle patient samples, as well as for clinician-scientists at the LIH-DII site. The aim is to achieve excellence and become a world leader in the selected research areas. This, naturally, sounds overambitious because of the current lack of sufficient critical mass of clinician-scientists and shortage of collaboration with MDs. The new large approach called Clinnova Center of Excellence (for digital health and personalized medicine), if funded, however, may change the picture and provide a larger scope of interests at the national level and interactions abroad. Since Clinnova is being evaluated at the EU-level, and no decisions have been made yet, we have not included it in our evaluation. Also, the biobank (IBBL) will be of strategic importance for enforcing translational research in LIH-DII. The relation between LIH-DII and the IBBL was excluded from our evaluation as the role of IBBL will be covered in LIH's institutional evaluation.

**Recent strategic achievements.** Based on the previous evaluation in 2015, and thanks to the good leadership and dynamic nature of the institute, the LIH-DII has been able to promote many of the suggestions of the 2015 evaluation team. These included setting up a PI-based researcher system and a local version of a graduate school for PhD students (called NextImmune). Attempts to focus the portfolio of research topics have also been made, but this has been under continuous challenge because of changing interests of researchers and the recruitment of new PIs. Nevertheless, the new recruitments have been very successful by bringing in more research spirit, activities and impact.

**Department structure.** The department PI system has been relatively clear during the period 2015-2018. Individual groups were divided into themes related to infections (INF) or allergy/inflammation/immunology (ALL). There were 11 groups (INF1-4 and ALL1-7). Recently, however, some groups merged together so that, for example, groups working on infections constitute one unit called LuCID and those working in allergy have a group of Molecular and Clinical Allergology. This may obscure the previous clear structure, where each PI-led group was independent. A new "Incubator" unit was set up and reserved for investigators whose research needs more external support and/or a new productive line of research. The recent changes in the organizational structure has for some PIs caused uncertainty or confusion related to their role in the future profile of the department.

**Recruitments.** The LIH-DII has been successful in recruiting new top scientists (Dirk Brenner, Mahesh Desai, Feng He). Naturally, this has been a good strategic move that has broadened the scope of research topics in the department. By going deeper into mechanisms, this type of research has a higher impact and feeds on collaboration with other groups by bringing in new techniques, themes and modes of action. Work on basic functional mechanisms in immunoinflammatory diseases is one of the key

topics at the LIH-DII. It should bring in visibility, competitiveness, high level publications and external funding. Key indicators of performance have documented e.g. a clear rise in the number and quality of publications.

**Financial resources.** The LIH-DII receives a significant block grant from the MESR, which has increased almost 20% during the reporting period. The LIH-DII originally aimed to achieve an overall 60:40 funding ratio (MESR:External), which was reduced to 56:44 in 2017. The department and its investigators need to work hard to translate the increased research output into a bigger share of external funding (including competitive grants and contract research), which is now only ~44 % of the overall funding With only 21% of the overall funding coming from competitive grants in 2017, there is certainly still room for improvement.

**Technology.** The department has strong emphasis on developing and maintaining up-to-date technology platforms for research. It has been in charge e.g. of a well-equipped flow cytometry unit that also includes the CytoF instrument. Research work is strongly going into the analysis of so called "big data" using multiple "omics" techniques (genomics, transcriptomics, proteomics, metabolomics) that each have their infrastructure needs. In addition to the existing animal facility a gnotobiotic animal unit was recently set up for microbiome studies. It will be important to ensure stability in the personnel leading and running these cores (cf. recent issues with the cytometry facility), and to keep the units accessible to all researchers at a reasonable price (currently applied prices seem too high). When units serve a larger set of customers it is advisable to have them functioning as separate core facilities from individual departments. In any case, for a smooth running of the core units financial support at the institute level is needed, in addition to expert personnel to get most out of expensive equipment. There is a specific need for a bioinformatics specialist to handle large datasets in a proper manner.

**Focus.** Despite attempts to focus research, LIH-DII still has a wide range of research topics. The main reason for this is the wide interests of the individual research groups. Considering its size, it is apparent that the LIH-DII should keep its major efforts on topics that have the highest impact value in science itself and for the Luxembourgish society. Nevertheless, the interests of individual researchers should always be appreciated, because they should have the best knowledge in their fields. Since the LIH-DII is a department for studies in infections and immunology it is natural that the existing themes of viral infections, allergy and immunology should all belong to the focus areas.

**Infectious diseases.** LIH-DII has a strong history as a service provider and surveillance unit in infectious diseases. It acts as a WHO collaborative center and a reference center for monitoring measles and rubella. Because of e.g. the recent measles epidemic in Europe, due to lack of appropriate vaccine coverage, this is a very important activity that should be supported and continued. Other challenges for the unit have been the emergence of new epidemics of viral diseases internationally and research on local problems related to HIV and HCV infections. These are functions that could be performed in collaboration with the Department of Population Health. It is, however, important to note that surveillance and public health functions must be based on scientific research and that this role should be facilitated by LIH-DII, which as such fits neatly in the translational strategy of LIH as a whole. It was felt by the review panel that the position of DII-INF is under pressure and that support from the block funding is at risk. However, for a stable continuation of the public health role of DII-INF it was thought to be important that DII-INF gets continued support for research in the field of infectious diseases, also because externally DII-INF has been the most visible part of the department for a long time. Very valuable and "down-to-earth"-type fruitful practical work with societal impact has been performed e.g. by teams of Drs Devaux, Hübschen and Muller. Also, collaborations with the recently recruited PIs should be encouraged (e.g. the effects of HIV on T cell metabolism, or the role of the microbiome in intestinal health). A feature not to be ignored is the possibility that infections can have an important role in either inducing autoimmune and inflammatory responses or in generating tolerance against them. Mechanisms mediating these effects are still obscure and thus worth investigating in collaboration between different research groups.

Emerging antibiotic resistance is one of the biggest threats to mankind. The strategy of LIH-DII mentions the selection of target pathogens *Mycobacterium tuberculosis* or *Pseudomonas aeruginosa*

for investigation. These bacteria often are resistant or develop resistance to multiple antibiotics. While studying bacteria would fit within the scope of a department for infections, there is not much tradition in this area. Proper research on this topic would necessitate very close links to the hospital and patients, a special unit to study pathogenic mycobacteria and experts in the field. Therefore, the LIH-DII may consider whether it indeed has the resources to expand into this area. Continuing work on viruses, as well as new collaborative research in the context of the recently initiated work on microbiomes would appear more natural.

**Immunoinflammatory diseases and cancer**. A new strategic research axis focusing on biomedical aspects of gut and brain was introduced during the evaluation. This fits well with newly emerging themes on immune mechanisms in inflammatory diseases of the gut and brain, the development of tolerance or allergies against food allergens, as well as the role of gut flora in the interplay between the gastrointestinal tract and the central nervous system (known as the 'gut-brain axis'). Importantly, as the population is aging, the numbers of patients suffering from intestinal inflammatory diseases and neurodegenerative diseases is steadily increasing and the underlying basic mechanisms are still not yet well understood. The LIH-DII strategy cites WHO non-communicable disease (NCD) burden as an argument to do research in this area. However, it is only the immunoinflammatory diseases that should be considered from the vast number of NCD. Therefore, the reasoning behind LIH-DII's focus should be better defined. With respect to LIH-DII's research in oncology, aspects related to the roles of inflammation in promoting cancer as well as immunotherapies could provide a basis for collaboration with LIH-DONC. A revolution is taking place in the development of new therapies directed at improving the immune attack against tumors with the so-called "check-point"-inhibitors and with monoclonal antibodies. Specifically, studies related to the metabolic activity of immune cells in killing tumor cells or tumors originating from immune cells seem particularly relevant in this field. For several of their cancer-related projects, LIH-DII is already collaborating with LIH-DONC. In the future, more of these transversal research topics may be defined in LIH where PIs from various departments work on in a collaborative effort (which could be enforced by a kind of 'collaborative program' budget from LIH).

**Allergy.** Another line of research with long tradition at LIH-DII and its predecessors relates to allergy. The increasing incidence of allergies, including responses to dust and molds, air pollution and food components, is an important medical problem. Allergic diseases are related to lack of immune tolerance and/or excessive and misdirected immune reactivity. It will be important to continue this line of research at LIH-DII not only because of the previous expertise (Drs. Hilger, Kuehn, Ollert), but also because the newly recruited PIs are very well placed to help in studying the basic underlying mechanisms (Drs. Desai, He, Brenner). The practical diagnostic and therapeutic applications are within reach in this type of work and aligns well with the current strategy towards translational research of the LIH-DII.

**IPR.** LIH-DII has established a strategy emphasis on promoting commercialization of research outcomes. In this context, the evaluation panel was somewhat surprised to learn that research results in the form of manuscripts or abstracts are to be sent to LIH's Intellectual Property officer well in advance of publication in order to evaluate the possibility for new patent applications. While it is important that new discoveries or products with potential for new biotech companies or licensing into existing ones are being evaluated, one should be realistic. It is only rarely possible to take research outcome into commercial products. Filing patents has little value in itself. If the product cannot be exploited, there will be loss of effort, time and money. The researchers may feel intimidated if the publication of their research is blocked or becomes delayed by the process of internal evaluation. Thus, the evaluation system should be more flexible and initiated primarily by the researchers themselves.

## 2.2 DII clients and stakeholders

During the peer review interviews took place with representatives of various internal and external stakeholders and clients of LIH-DII. Interviews took place with the following groups:

1. *PhD students and post-docs.*

A face-to-face informal discussion took place with 7 PhD students and 3 post-docs. The discussions were very open and frank and the picture that emerged was that of an enthusiastic group of early-stage researchers that had found their place at LIH and more specifically at LIH-DII, allowing them to develop their research skills in an environment with very appropriate expertise and facilities. However, a number of issues were raised that they would like to see addressed:

- More clarity for PhD students on what the requirements are for obtaining a PhD. Officially the PhD students should comply with the requirements of UL or their affiliated university but at the same time LIH-DII has its own (stricter) requirements.
- An issue that was shared by the majority of the PhD students and post-docs was the uncertain career perspectives in science, in particular in Luxemburg. More coaching was felt to be needed.
- Some PhD students also felt that they are at the bottom of the pyramid and that there was too little attention to their problems and needs. This was in particular experienced at the start of NextImmune, when very little infrastructure for the PhD program was in place. In some cases, PhD students could actually not start their project because the necessary materials (e.g. specific mice) were not yet available.
- It was felt that the mission of LIH-DII was not always clear and that it changed too often. Better communication is needed in this area.
- It was also seen as a problem that LIH-DII has poor visibility to the outside world, which decreases the career chances.
- LIH-DII was seen as an archipelago of independently operating research groups with little synergy brought about by the PIs. It was felt that in fact, PhD students and post-docs were more successful in interacting at the department level than the PIs.
- LIH-DII offers excellent opportunities for big data collection, but the facilities and support for data analysis (bioinformatics) are suboptimal.
- For collaborative projects between LIH-DII and OUH (Odense) administrative hurdles were experienced and the way towards double affiliations has not been worked out.
- PhD students have a voice through a PhD representative but it was doubted whether this voice is really heard.
- Training of PhD students was thought to be more effective if more post-docs were available.

2. *Other stakeholders:*
   - Roche Medical Diagnostics
   - Development Cooperation Office (Vientiane, Laos)
   - Health Directorate of the Ministry of Health (MSAN)
   - LCSB (University of Luxembourg)
   - Animal Facility (University of Luxembourg)
   - Centre Hospitalier de Luxembourg (CHL)

Overall, the feedback of all the different stakeholders was very positive. A few aspects were mentioned that should get some attention and/or could be improved:

- The speed of administrative processes, i.e. contracts etc., was thought to sometimes be sub-optimal.
- Some concern was communicated about the future of the international collaboration with South-East Asia when Dr. Muller would not be involved anymore, but there was trust that there are competent qualified researchers at LIH-DII that will step in.

- DII is now the WHO reference centre for measles and rubella but there is some uncertainty whether LIH-DII can become such a centre for a number of infectious diseases for Luxembourg. It would have preference that LIH-DII takes up the role of national reference centre for infectious diseases to avoid that contacts with LIH-DII will become indirect (e.g. via LNS).
- It was indicated that sometimes communication about contracts for collaborations is not optimal, making the process slower than necessary. Perhaps a more direct decentralized involvement of PIs involved would make the process more efficient.
- The UL-Animal Facility is housed next to the LIH-DII. The fact that LIH-DII also uses another mouse facility run by LIH-DII itself can cause some issues as a quarantine period for people working in both facilities has to be taken into account. Also the extra administration associated with the invoicing and payment of the delivered services between LIH and UL was mentioned. Recently, UL and LIH-DII jointly started a germ-free mouse facility, which is a unique facility in Luxembourg and which is expected to be key for future research in LIH-DII. It also puts LIH-DII in a good position for collaboration with other laboratories and pharma industry who is also interested in such services.
- The CHL is a key partner for LIH-DII in research and training. The future plan to set up MD training for the 3 first years of the curriculum, i.e. the preclinical studies, was discussed. LIH-DII would be part of this, although major emphasis is on oncology and neurology. Because of the latter, LIH-DII should aim to play an active role in planning the curriculum and provide teaching in microbiology and immunology. CHL has 2-3 infectious disease experts, but medical specialist training is usually done abroad. Currently, CHL and LIH-DII have many collaborative projects, around 10 ongoing and 5 in preparation. These are mainly studies in the field of allergy (Ollert/Kuehn/Hilger) and viral infections, like HIV and HCV (Devaux). In general, the collaborations have gone smoothly. The distance between CHL and LIH-DII was not felt to be a major problem, because samples could be transferred relatively easily to LIH-DII. From the CHL side 2-3 clinicians (e.g. Martine Morrisset) participated in the studies. Access to patient samples has been organized smoothly. A key point for researchers is to note that the hospital is more than a sample provider for the researchers, i.e. work is done in collaboration. Clinician scientists at CHL have been happy with the collaborations. The existing shortage of MDs at LIH-DII is a problem for the transition of LIH-DII to a more translational direction. The planned Luxemburg Center for Translational Research, involved in performing initial phase I trials for drug candidates, is a good step in the direction of resolving this problem, together with 3 planned clinician scientist positions. The first one of these, with an 80:20% ratio, hospital:DII, is in the process of being filled. In the future, more than these three positions are needed, because the shortage of MDs at LIH-DII is, and is likely to remain, a problem. With respect to the collaboration with CHL there is another problem, which is that collaborations are usually based on LIH-DII funding or on FNR grants, because CHL does not get governmental funding for research. This has led to a situation that CHL lacks capacity for research in the fields of immunology and microbiology. The employment of three clinician scientists will be a significant improvement, but this should be supported by further infrastructure for translational research (e.g. research nurses, pharmacy facilities, clinical trial support etc.)

Overall, the interviews gave a very positive impression of the performance of LIH-DII with its internal and external stakeholders and clients. The issues raised by PhD students and post-docs are not unexpected in an organization that has just started to develop a PhD program. Extra attention has to be given to improve this situation. A recurring topic for improvement was the speed and organization of administrative processes.

# 3 Assessment of LIH-DII

## 3.1 Research quality

The key research output of LIH-DII are peer reviewed publications in international research journals, reporting new insights in basic mechanisms or technology development. We therefore have judged the overall quality of scientific output on the basis of the quality and quantity of the papers published, the technical know-how, and the plans for future research as presented by the PIs.

Part of the activities of the LIH-DII are however focused on providing premier service and acting as a national focal point for preparedness, and surveillance in infectious diseases for several governmental and non-governmental agencies. The review panel would like to highlight the importance of embedding these activities, which are of great importance for public health in Luxembourg, in a setting where continual basic research in the field of infectious diseases takes place.

Overall, the committee was positively impressed by the state of research presented, by the publications and the quality of the PIs and students. Most PIs are doing highly competitive research on an international level and offer the opportunity to contribute at top level to the scientific community. The quantity and quality of research publications authored by LIH-DII has increased during the evaluation period, in part by the new recruitment of a number of well-performing PIs. Nevertheless, with a few exceptions, the actual output of most PIs in first and senior author research publications is still limited, the more if one takes into account the relatively high input (both in human and financial resources). A major research focus is on the molecular and cellular mechanisms that control immune responses in the context of infectious and inflammatory diseases, organized in two basic research units, the Infectious Diseases research unit and the Allergy – Immunology – Inflammation Research Unit. These topics are of high medical relevance and put the LIH-DII in a good position to contribute to the new mission of LIH to impact on patients in addition to performing fundamental biomedical research.

The committee did not assess the performance of each PI and group individually, but rather the performance of the two research units to which these groups belong. In the following paragraphs some remarks are provided about the functioning of the two research units of LIH DII.

### *3.1.1 Infectious Disease Research Unit*

The Infectious Diseases research unit at LIH-DII has been managed by Prof. Claude Muller with the Deputy Head Dr. Carole Devaux. Recently they acquired a new brand name LuCID, Luxembourg Center for Infectious Diseases and Prof. Muller has retired. Other PIs at the Unit are Drs. Judith Hübschen and Dr Danielle Perez Bercoff. In addition to doing research, the unit serves the government of Luxembourg (Ministries of Health, Agriculture and Foreign Affairs) and acts as one of the three WHO reference centers for measles and rubella surveillance in Europe. In addition, LuCID has collaboration with the Pasteur Institute and is linked to the ECDC network. The main emphasis is on viruses. Work on bacteria or parasites is practically absent from the unit. The unit has biosafety level (BSL) 2 and 3 laboratories. The latter is in connection with the animal facility.

LuCID acts as a national reference laboratory for HIV and hepatitis C-virus infections. This includes collecting and analyzing information as well as maintaining relevant registries and databases. The unit carries out the follow-up of HIV- and HCV-infected patients in Luxembourg by doing laboratory analyses, e.g. molecular typing. There are also studies on HIV drug resistance and latency and viral and host factors that regulate HIV transcription and cellular signaling. The laboratory is well known in Europe because it has contributed to the design of action plans to combat diseases caused by these viruses. In Luxembourg the lab monitors drug resistance of HIV and HCV. Work includes also monitoring these infections in i.v. drug users. This is an important activity with impact.

LuCID has a number of national and international collaborations. Most of the patient material originates from the hospital (CHL). In this collaboration the distance has not been seen as a problem. There is a reasonable amount of external funding for multiple collaborative projects. Recently, however, external funding in the current evaluation period seems to have decreased.

The publication output of LuCID is relatively good, although mostly based on collaborations and not published in the highest impact journals. In the future, it might be advisable for the LuCID to take a stronger role in the studies the group is performing. One interesting joint patent has emerged from the work. Researchers have developed multimer immunotherapeutic complexes based on the complement C4bp protein. These were originally aimed at being a therapeutic agent for HIV but have more recently been designed for therapy of human B cell lymphomas. There is also interesting work on Avian influenza and Newcastle virus diseases. The unit has been able to explore and contain a recent avian influenza epidemic that originated from Belgium.

LuCID is strongly involved in capacity building in the third world, like in Africa and Asia. Most of the international activities were initiated by the former head of the unit, prof. Claude Muller, who recently has formally retired but apparently still will continue many of the existing activities. There is particularly active training of people with different backgrounds in Europe, Africa and Asia (Laos). Most of this was in connection with work on measles and rubella, two major vaccine preventable diseases of global significance. In line with the "One Health"-concept LuCID carries out work both on animal and human disease agents, e.g. with different types of influenza viruses.

As a whole LuCID is doing a significant amount of work in important areas. This work is not always reflected in scientific publications. Behind the public health aspects there is, however, a considerable amount of basic research that belongs to the profile of LIH-DII. Relative to its activities the unit is small, currently only 2-3 main PIs. Thus, the unit would need to be strengthened possibly by a new recruitment or collaboration with other units. For an infectious disease unit the LuCID laboratory is also of narrow scope. In this context, more collaborative work on bacteriology and microbiomes could now be done with the DII-ALL unit, where interesting work on host/gut microbiome interactions has been initiated. In any case, there is a need for further support and acquisition of external funding. The recent successful application for a doctoral training unit by the FNR DTU PRIDE Scheme « Microbiomes in One Health » (https://microh.uni.lu/) in 2017, for which 17 PhD students and 2 post-docs were granted from 2018 onward (6 PhD students for LIH, 5 within LIH-DII) may provide a good platform for this.

### *3.1.2 Allergy – Immunology – Inflammation Research Unit*

The DII-ALL unit is clearly the unit with the highest critical mass and serves as the flagship of the LIH-DII. The unit is managed by Dr. Markus Ollert as ad interim head, with Dr. Christiane Hilger and Dr. Jonathan Turner as deputy heads. In the evaluation period the unit comprised 7 research teams, each led by 1 or 2 PIs (including 3 newly recruited PIs) and each having their own research line that fits into the general scope of the unit. From August 2018 onwards, however, the unit has been restructured into 6 teams each led by 1 PI, except for the Molecular and Clinical Allergology team that has 3 PIs. In addition, an incubator group has recently been formed in which 3 PIs whose research groups were discontinued have been regrouped and are now trying to redirect their previous research into a number of new research lines.

The research topics of each team fit the general mission of the LIH-DII but are still rather diverse and independent of each other. Further efforts to further streamline the variety of research subjects (neuro-inflammation, cancer immunology, immuno-aging, allergology, behavioural immunology, gut immunology), which will also enable more collaboration between DII-ALL groups, will be needed. This will also increase the overall visibility of the LIH-DII. In this context, the planned establishment of a new group 'Neuroimmunology' should be critically reconsidered if really necessary and appropriate. In view of the changing mission of the LIH towards more patient-oriented research, the panel was happy to see that all PIs referred to possible strategies for their integration in LIH transversal and cross-sectional topics and translational activities.

The DII-ALL has set up strategic collaborations with several national and international partners such as the Odense Research Center for Anaphylaxis at the University of Southern Denmark (where Dr. Ollert is affiliated as full professor), the RIKEN Research Center in Yokohama, the Centre Hospitalier in Luxembourg, the LCSB unit at the University of Luxembourg, and many others. They are actively involved in the NextImmune Doctoral Training Unit (DTU) and are hosting several PhD candidates.

Also the involvement of DII-ALL researchers in establishing the world's first exhaustive handbook on Molecular Allergology deserves special attention.

The research performance of the DII-ALL is very good, both in terms of productivity, scientific quality and impact. The number of publications published in the best quartile of the respective journal category and among the top 10% in the field improved significantly in the last 4 years, with several pivotal publications in top journals, although the number of 'own' (first or last authorships from DI-ALL) research papers should still increase relative to the input of human and financial resources. In general all PIs of the DII-ALL are internationally visible, with some of them being strong players on the international stage and having the potential to be among the best in the world in their respective field. In this context, the work of 2 PIs deserves special attention. Research of the group of Dr. Dirk Brenner is clearly at the frontline of immunology and recently published work in the prestigious journal 'Immunity' describes a paradigm shift in the metabolic regulation of T cells with a big potential impact for the treatment of immunity and cancer. These findings offer great opportunities for the group's and DII's future developments aiming to study novel concepts of metabolic regulation. Also the work of Dr. Mahesh Desai, a young scientist who was recruited from the University of Michigan, deserves a special mentioning. Their finding that dietary fibre deprivation leads to thinning of colonic mucus and increased pathogen susceptibility in mice is seminal as it demonstrates previously unknown mechanisms explaining the intricate link between food, the microbiome and intestinal health. These findings were published in the top journal 'Cell' and received a world-wide press coverage and has already been cited many times by other scientists. These strong PIs are well positioned to determine, together with the director, the future strategy of the department and to bring more focus.

Specific efforts will be needed to increase the tech transfer output of the units (in terms of patents and licensing agreements). Collaborations with industry are present but are still limited in terms of scope and size. The collaboration agreement with Confo-Therapeutics on a project aiming to develop new innovative tools in the context of an immune receptor investigated by the team of Dr. Andy Chevigne is of high interest. Also an agreement with a large private diagnostic laboratory in Luxembourg on the development of a diagnostic allergy test and other allergy-related topics are worth mentioning. The panel saw several research subjects (e.g. related to chemokine receptor antagonists, or allergen specific immunotherapy) that have big potential for future knowledge transfer towards medical applications. Also, given the planned strategic focus towards more applied and patient-directed research, as well as the Clinnova project that is under review, tech transfer should not be a major problem in the future.

All PIs of the DII-ALL seem to have sufficient financial and human resources to do their research. Besides the block grant from LIH, they were able to obtain competitive funding. However, it was striking to see that most of this competitive funding came from FNR, with limited or no funding from European grants. Given the high level of some of the PIs, also individual grants from the ERC program are certainly feasible and should be promoted.

In conclusion, by all important parameters, the DI-ALL has been doing very well. There is a proper emphasis on quality over quantity and altogether a sign that the unit is increasing its ambition. The panel was impressed by the different ideas and initiatives that are present at different stages of maturity. All forces should now pull together to make the LIH-DII stand out internationally.

## 3.2 Innovation quality and impacts

In line with LIH's mission statement, LIH-DII's mission statement is focusing on "translating basic science into clinical practice for improved health care", i.e. research with measurable impact on patients (answering unmet medical needs). As part of this strategy, LIH-DII has implemented a mechanism to monitor all research very closely with respect to patent opportunities. Patents are positioned as a good indicator of the quality of the innovation impact of the department. As a logical next step, the innovation impact is judged by subsequent valorisation and commercialisation of the newly acquired intellectual property. This includes the set-up of spin-off companies and the development of market strategies. Here we try to establish how effective this strategy has worked out, without judging whether this very strong

focus on translational research with measurable valorisation is the best choice for a governmental research institute.

In two areas a number of patent applications have been filed, one in the field of cancer (multifunctional hetero-multimeric constructs) by researchers from LuCID (Carole Devaux et al.) and three in the field of allergy (tolerance promoting adjuvants and vehicles for allergen immunotherapy).

For the first innovation in the field of cancer treatment, FNR-Proof of Concept (PoC-JUMP) funding has been obtained. The innovation is a result of collaboration with the University of Reims (France), and the project has, in addition to the FNR PoC-JUMP grant, also received a French governmental grant to investigate bio-availability, toxicity and pharmacokinetics in laboratory animals, an essential step prior to clinical testing in humans. These developments can certainly be seen as successful promising steps towards valorisation of innovations with potential impact on patients' health. Prerequisite for further steps in possible clinical development is availability of the planned Phase I clinical trial centre. If future results are promising, it should be carefully evaluated what partnerships (clinical and commercial) are needed to proceed towards Phase II studies.

The inventions in the field of allergy (anti-inflammatory adjuvants, hydrogel-based formulations for allergens, methods for immunotherapy) have resulted in the establishment of a spin-off company (Tolerogenics) of which LIH-DII director Markus Ollert is scientific co-founder and Chief Medical Officer. The medical needs in the field of allergen immunotherapy are to 1) increase safety, 2) to assure long-term tolerance, and 3) to decrease the duration of the treatment. There are no publications to evaluate to what extent the innovations of LIH-DII may contribute to these medical needs. Over the past two decades many attempts have been made worldwide to improve the performance of allergen immunotherapy along these lines, but so far none have been successful, usually failing in Phase III (or not even proceed towards Phase III) or failing to provide sufficient support for significant benefit compared to existing registered immunotherapies, thereby not justifying further large investments. So, the potential impact of the innovations of LIH-DII/Tolerogenics is hard to judge without insight in the pre-clinical data obtained thus far. It can be anything from very high potential to "one extra initiative that does not provide real benefit compared to what is already on the market". The only way forward is to publish the pre-clinical data and to evaluate whether development of a program for future human clinical testing is warranted. The new clinical translational centre will be essential to facilitate such a (possible) clinical development program.

The above evaluation of the innovation impact is along the lines of the valorisation-driven mission statement of LIH-DII. It is however important to have a broader look on the impact of LIH-DII on patient health. The LuCID group of Carole Devaux has an important position in surveillance of infectious diseases in Luxembourg to allow health care to be able to respond rapidly to health threats for the Luxembourgish population. In addition, the group serves as WHO reference laboratory and it promotes improvement of health care in Laos and other developing countries. The value of these contributions should not be underestimated and is a good reason for LuCID to remain embedded in LIH-DII. In addition, LIH-DII provides a good scientific environment for LuCID to continue basic research in the field of infectious diseases.

## 3.3 Management and governance

LIH-DII was created in 2014 by a fusion of LRTV and LIGA. The review panel unanimously agreed that the director of LIH-DII has demonstrated strong and effective leadership over the first three years of LIH-DII's existence.

At the start LIH-DII consisted of two main units, one for Infectious Diseases (DII-INF) and one for Allergology, Immunology and Inflammation (DII-ALL). DII-INF housed 4 PI groups, and DII-ALL 7 PI groups. In response to the advice to limit the diversity in topics, coming out from the external review in April 2015, some PI groups were merged together recently (January 2018). Three of the four DII-INF groups were merged into LuCID, one was moved to DII-ALL. In DII-ALL, the two allergy PI groups were joined, and one group was discontinued due to insufficient performance in obtaining competitive grants. The PIs of the latter group were placed in a so-call Incubator group for Early Projects. The peer review

panel judged the reduction in variety of research topics (as advised in April 2015) very limited, because all PIs continued to work on the same topics. In fact, the only change implemented was that in DII-INF three PIs/topics were joined in one organizational group, and the same happened to two PIs/topics in the DII-ALL unit. Although the review panel agrees that evaluation of PI performance in a PI-based organization is of great importance, and underperformance should ultimately have consequences, it was not very happy with earmarking underperforming PIs with a label ('incubator group'). It was thought to be more appropriate to keep their status as independent PIs and groups, while re-focusing their research strategy and efforts, and setting clear well-defined objectives for a re-evaluation after a predetermined period of time. Also, a clear phasing out strategy for the PI should be agreed on in advance in case this re-evaluation would be negative. In any case, leaving underperforming PIs with "a sort of second rate earmark" should be avoided. It was also felt that there is no clear set of performance parameters available for PI evaluation, or at least that the peer review panel could not distill this from the documentation or the review meeting. The peer review panel advises to establish a clear protocol for PI evaluation and communicate this to the organization.

One of the other advices of the 2015 review was the creation of a PhD program. The peer review panel was impressed about the successful implementation of the NextImmune Graduate Program. Clearly, there were some start-up problems but overall, LIH-DII has been very effective in setting up the program. The separation of LIH-DII and LIH-DONC over two locations, is one of the problems which significantly hampers optimal synergy and collaboration between these two departments from which the PhD program could benefit. In light of that, the peer review panel is a strong supporter of the creation of a Biocampus in Esch-Belval, hosting both LIH-DII and LIH-DONC. It is relevant to notice here that the CEO and CFAO report separately to the Executive Committee, and that they are not aligned with respect to a move of LIH-DONC to Esch-Belval. This situation is considered detrimental for executing an effective strategy to create a Biocampus.

Another success of the past years is that LIH-DII has been successful in attracting a number of high potential researchers. This has resulted in the establishment of successful research lines with publications in high impact journals such as Cell and Immunity. It will be a challenge for the future to keep these top researchers in Luxembourg. Better profiling of LIH-DII (and LIH as a whole) to the outside world, more success in international collaborations leading to acquisition of EU-funding, and last but not least support to obtain professorships at Luxemburg University, were considered essential by the review panel to keep a prolonged stay in Luxembourg sufficiently attractive.

LIH-DII has been very successful in setting up a state-of-the-art research facility with the National Cytometry Platform (NCP), a Proteomics Suite and an animal house with a facility for germ-free mice. These facilities provide PIs and their groups an excellent research environment. Two things deserve attention however. Firstly, big data collection facilitated by these cutting- edge facilities is not balanced by sufficient access to bioinformatic and statistical support. Although there are collaboration projects with LCSB, these connections do not provide data analyses services. LIH-DII is dependent on their too limited in-house bio-informatics support.

A second issue that deserves attention is the full cost model used for access to the core facilities. This is a too big burden for projects' budgets and a hurdle for grant applications that do not accept the full cost model. The LIH-DII management has ensured that the full cost model will be replaced by a marginal cost model. Another problem that was identified is the 25% overhead that LIH-DII charges over external funding. Some external clients like some of the Ministries working with LIH-DII do not accept 25% overhead, and do not want to cover more than for example 15%. This means that the PI in LIH-DII has to pay part of the overhead out of the project money needed to carry out the work or use the block grant to match the funding gap.

Another promising development mentioned previously which will facilitate implementation of the strategy of LIH to increase translational research is the creation of a translational clinical research centre and a Phase I clinical trial centre. On top of that, positions for up to three clinician scientists have been decided upon. These clinician scientists will have joint affiliations with LIH and CHL and thereby serve as facilitators of translational research. Already now 10 running and 5 planned collaborative projects

between LIH-DII and CHL exist. A clinician scientist with dual affiliation will give these types of collaboration a boost.

One of the most critical issues in management and governance is the poor state of the administration. Almost without exception PIs complained about the fact that management of projects, in particular their financial management essentially has to be done by the PIs themselves. Financial administration is in Luxembourg city and it is either unclear who the contacts for projects are and if a person is identified it remains very difficult to get contact. The peer review panel unanimously agreed that a financial administrator should be available on location in Esch-Belval. This will improve project management and allow PIs to spend their valuable time on research instead of financial administration.

The Executive Committee has decided to change budgeting from a bottom-up to a top-down approach. The argument is that the limits of the block funding have been reached and that the bottom-up approach became unaffordable. The review panel experienced that this recent change creates a lot of uncertainty in the organization. It was advised to communicate as soon as possible to the organization how budget division will be organized. Full transparency is needed to explain which parameters decide on the block funding division. It was considered a risk that groups will start seeing their colleagues as competitors. Of course, in a way this is the case, but it has to be clear what decides on the division. This clarity is urgently needed. It should be made clear that until the exact mechanism has been decided upon that the division will stay as it is.

From a management and governance angle it is also important to analyse why LIH-DII (and LIH as a whole) is so unsuccessful in acquiring EU funding. One explanation that came up that the level of block funding has long been a luxury situation in which acquisition of external (EU) funding was not absolutely necessary to survive as a PI. Now that the ceiling has been reached and a top-down division of block funding will be implemented, the motivation to go actively for EU funding will increase. Nevertheless, the review panel felt that it is absolutely crucial that a professional support office with people with experience in EU funding is created. All successful institutes have such offices. Without this support it is very difficult to become successful in this arena. The only large application to the EU that is still in the running phase is the Clinnova project. It is however uncertain whether the grant of 15 million will in the end be obtained. The peer review panel felt that LIH-DII should have a back-up strategy in case this grant is not awarded to LIH-DII.

Finally, the review panel felt that strategic objectives focusing on technology transfer and valorisation should be handled in a less rigid way. In this context, it was advised to soften if not completely strike out the requirement for all abstracts and papers to go through the tech transfer office (RKTO). It was felt that this hampers free communication amongst scientists and creates problems for PhD students and post-docs. If well trained and informed, PIs should hold responsibility to evaluate any confidentiality and/or patenting issues in their work, and can always ask advice from RKTO in specific cases if needed.

# 4 Conclusions and recommendations

1. The LIH-DII should continue the development of focus on themes covering common topics. The goal should be to foster collaborations between themes. At present, the groups seem to enjoy considerable freedom in pursuing their own plans, with little overall scientific management. To become a top institute that is highly visible and to adhere to LIH's mission, a strong LIH-DII management could be formed by a small group of researchers who head the groups working on the core topics of the department (allergy, immunometabolism, gut inflammation, and viral infections). This scientific management should set priorities, develop a vision and be held responsible together with the director, who would be the first among equals but responsible for reporting and organisation. The enhancement of synergy between research groups should be considered as main goal. It should stimulate concentration on chosen subjects and discourage broadening of the subjects being studied. Collaboration could be encouraged by providing proper incentives.
2. Although we have seen good intentions of all the PIs to focus on translational research and transversal themes important for LIH, in our opinion the PIs should continue high level basic research. They should increase their output by focusing their efforts on these aspects in which they are strong, validating their hypothesis in the right animal models and where possible by using patient-derived material. Implementing too drastic changes and focus all research of a group on 'translation' may be unrealistic and cause more harm than benefit. LIH-DII could use the new LIH mission towards translational and clinical research to its own advantage by using it to create focus in the variety of research topics, through the recruitment of clinical scientists, and the establishment of strategic collaborations, rather than performing a complete make-over of the research lines of the individual groups into translational research. In our opinion, a kind of 'transition state' should be possible, whereby LIH provides resources to bring findings/technologies one step closer to the clinic, without impeding the scientific drive of a research group.
3. Given the strengths of LIH-DII's PIs in basic research and its importance in driving translational research closer to the patient, we recommend to include basic research in the mission statement of the LIH-DII, which would just require adding the word 'performing' in the current mission statement (Inducing Immune Tolerance and Activating the Immune System for Human Health – Performing and Translating Basic Science into Clinical Practice for Improved Health Care)
4. In order to contribute to LIH's transversal and cross-sectional topics, we recommend to increase the LIH-DII budget reserved for strategic use, which may be used to set up strategic collaborations (intra- and interdepartmental), to invest in new technological developments, and to recruit more clinician scientists.
5. To enable the transition to a better translation of basic research findings into the clinic, collaborations with the clinic should be promoted and established early in the project. This will require a clear commitment at the side of the basic researcher, but also at the side of the clinicians. Therefore, proper incentives may be needed.
6. The director of LIH-DII, together with all other LIH directors, the LIH management and stakeholders, should make all necessary efforts to ensure a biomedical campus becomes reality.
7. To motivate researchers, to develop career tenure tracks and to recruit new MD/PhDs a local academic structure should be set up. LIH-DII should be actively involved in the development of a Medical Faculty for preclinical studies (especially in immunology, allergology and microbiology) and get prepared for related teaching duties.
8. The LIH-DII's role as a service provider and surveillance unit in infectious diseases could be performed in collaboration with the Department of Population Health. It is, however, important to note that surveillance and public health functions must be based on scientific research. The director should therefore consider if he wants to play an important role in this and develop infection related research further in LIH-DII. In this context, known links between infection and inflammatory diseases may offer some interesting opportunities to focus on.

9. As unclarity in financial management and related communication at the LIH level has been a complaint by all PIs, leading to frustration and difficulties in planning research, we strongly recommend to make financial administration available and approachable on-site. At the same time, the doors and ears should be kept open for the concerns of individual investigators.
10. As matched funding from European grants is very limited, we recommend to install incentives that promote the application for H2020 project grants and individual ERC grants. In addition, more professional support for applying for EU/international grants is important to increase the success rate.
11. The transition from a bottom-up funding policy to a top-down funding policy of the research groups has created quite some uncertainty among the PIs. More clarity and communication on the implementation of this new policy and the criteria that will be used is urgently needed. Together with this, a transparent evaluation structure needs to be developed and communicated to all people working in LIH-DII. The division of MESR block funding should include competitive elements (for example the necessity to bring in matched external funding, a set number of publications), but should also recognise and appreciate the strengths of the groups that have a high societal or economic impact (versus scientific impact only).
12. For a smooth running, the core facility units need financial support at the institute level, and expert personnel to get most out of expensive equipment. The services that are provided should be made available at marginal costs.
13. Project management and financial control are now mainly done by the PIs themselves. Responsible persons in Luxembourg city are not easily accessed. It is advised to employ a project manager/controller on site in Esch/Belval to support PIs.
14. The committee noticed a special need for support in bioinformatics and statistics to handle large datasets in a proper manner. As support from LCSB is limited to support in the context of research collaborations, the LIH-DII should consider the recruitment of new staff that can bring in this expertise.
15. The national cytometry platform is the technical jewel of LIH-DII. It should be maintained professionally and with clear policies (including reasonable prices) to customers and collaborators. It may serve best in its functions as a separate core-facility of the LIH.
16. While the PhD training has now been well set up, the next challenge is to prepare a plan to accommodate post docs into the research system, which should ensure that key expertise and guidance for the PhD students is kept in the department.
17. The committee strongly recommends the fast and clear communication of the changing strategy and organisation of the department at all levels, as there seems quite some unnecessary uncertainties.
18. Better communication and coaching of the PhD students is needed on the requirements for obtaining a PhD and on the career perspectives in Luxembourg after a PhD.
19. We recommend to at least soften if not completely strike out the requirement for all abstracts and papers to go through the tech transfer office (RKTO), and to make PIs responsible for this. The role of RKTO should focus on looking for prior art and providing fast and appropriate support in writing the patents and formulating the right claims, keeping in mind that time should only be spent to patents that have a real chance for return of investment and economic or societal impact.

# Appendix A Members of the Assessment Committee

Rudi Beyaert (Chairman):

Rudi Beyaert is full professor at the University of Ghent (Belgium) and Deputy Director of the Center for Inflammation Research at the VIB, a life sciences research institute in Flanders. He is heading the Unit of Molecular Signal Transduction in Inflammation, whose mission is to study the molecular mechanisms that regulate inflammation and immunity. Prof. Beyaert's scientific research is situated at the borderline between molecular biology and medicine, and makes use of a variety of modern biochemical, molecular and cellular approaches combined with mouse gene targeting and mouse models of human inflammatory disease. So far, he has supervised 37 PhD students and more than 30 postdocs, of whom several now hold professor positions while others made their careers in industry, public health, clinical reference laboratories, etc. Prof. Beyaert has published over 250 research papers that received more than 17 000 citations, which is also reflected by a h-index of 69, and he is inventor on >10 patent applications. His work has been recognized by a number of awards, including the five-yearly Prize of Fundamental Medical Sciences of the Belgian Royal Academy of Medicine.

Seppo Meri:

Professor Seppo Meri is Professor of Immunology at the Medical Faculty, University of Helsinki, Finland and the Chief Physician of Research in Microbiology at HUSLAB, laboratory of the Helsinki University Hospital. His medical speciality is in Clinical Microbiology. He served as a postdoctoral fellow at the University of Texas in 1988 and in 1989–90 as an EMBO fellow at MRC, Cambridge, UK. His research interests include diseases related to disturbances in complement regulation, pregnancy disorders, vascular damage and reasons for increased susceptibility to microbial infections. He has published over 250 original research articles and 130 reviews or textbook chapters on complement, autoimmunity and microbial escape.

Ronald van Ree:

Ronald van Ree is full professor of molecular and translational allergology at the Academic Medical Center of the University of Amsterdam (The Netherlands). At the Departments of Experimental Immunology and of Otorhinolaryngology he leads the Laboratory for Allergy Research. In his research, Prof. Van Ree focuses on the role of allergen molecules and environlental co-factors in the process of sensitization, tolerance induction and symptom elicitation. These studies include epidemiological field studies in Europe, Asia and Africa, and experimental animal models of allergic diseases and immunotherapy. Translational studies focus on molecular approaches for allergy diagnosis and immunotherapy. Prof. Van Ree has participated in many EU Framework Program projects since FP4. He has coordinated five large collaborative projects. He has been Vice-President for Congresses in the Executive Committee of the European Academy of Allergy and Clinical Immunology (2013-2015). He is on the editorial board of several leading journals in the field of allergology, and has ben associate editor of International Archives of Allergy and Immunology. Ronald van Ree has published around 320 papers in peer-reviewed journals, and several book chapters. His h-index currently is 64, with 13.500 citations.

# Appendix B Site visit programme

Day 0 (no presence of LIH required) – September 18

| Time | Programme | By |
|---|---|---|
| late afternoon, early evening | Arrival of peers in Luxembourg | |
| 19:00 – 22:00 | Get together of the panel (over dinner), inform peers about peer review goals and approach, presentation of preliminary analysis | peers, client (MESR) |

Day 1 – September 19

| Time | Programme | By |
|---|---|---|
| 08:30 – 09:00 | Transfer to institute: rue Henri Koch, 29, Esch-sur-Alzette | |
| 09:00 – 11:15 | General introduction to the Institute and to the Department of Infection and Immunity (DII) (and critical self-assessment of the department)<br>Discussion | **Dr U. Nehrbass** -Director LIH<br><br>**Prof. Dr. Markus Ollert** – Director, DII and PI, Molecular and Clinical Allergology<br><br>In presence of:<br><br>Dr. Frank Glod-<br>Chief of Scientific Operations, LIH<br><br>**Prof. Dr. D. Brenner**- PI, Experimental and Molecular Immunology Group, Deputy Chair, Research and Strategy, FNR ATTRACT Fellow<br><br>**Dr. Carole Devaux** – PI, LUCID, Deputy Chair, Quality and Safety<br><br>**Dr. Andy Chevigné** – PI, Immunopharmacology and Interactomics Group, Deputy Chair, Academic Affairs<br><br>**Dr. Jonathan Turner** – PI, Epigenetics and Behavioral Immunology Group, Deputy Chair, Finance & Funding<br><br>**Dr. S. Delhalle**-Scientific Advisor and Project Coordinator |
| 11:15 – 12:30 | Tour around the Department of Infection and Immunity | |
| 12:30 – 13:30 | Lunch at the Restaurant House of BioHealth | **U. Nehrbass,**<br>**F. Glod,**<br>**M. Ollert,**<br>**D. Brenner,**<br>**C. Devaux,**<br>**A. Chevigné,**<br>**S. Delhalle,**<br>**J. Turner** |
| 13:30 – 15:15 | Presentation and discussion on research theme 1 'Acute and chronic inflammation', based on max. 40 min. short presentations<br><br>13:30 – 13:40<br>Immunometabolism | **In presence of:** |

| | | |
|---|---|---|
| | **Prof. Dr. Dirk Brenner** – PI, Experimental and Molecular Immunology Group, Deputy Chair, Research and Strategy, FNR ATTRACT Fellow<br><br>13:40-13:50<br>Immune receptor networks and functions<br>**Dr. Andy Chevigné** – PI, Immunopharmacology and Interactomics Group, Deputy Chair, Academic Affairs<br><br>13:50-14:00<br>From gene network to immunoaging<br>**Dr. Feng He** – PI, Immune Systems Biology Group<br><br>14:00-14:05<br>IL-13 and Parkinson's disease<br>**Dr. Tatiana Michel** – PI, Incubator Group<br><br>14:05–14.10<br>Human Natural Killer (NK) cells: Hope for Immunotherapy of Cancer and Infections<br>**Dr. Jacques Zimmer** – PI, Incubator Group<br><br>14:10-15:15 General Discussion | **Prof. Dr. Dirk Brenner** – PI, Experimental and Molecular Immunology Group, Deputy Chair, Research and Strategy, FNR ATTRACT Fellow<br><br>**Dr. Andy Chevigné** – PI, Immunopharmacology and Interactomics Group, Deputy Chair, Academic Affairs<br><br>**Dr. Feng He** – PI, Immune Systems Biology Group<br><br>**Dr. Tatiana Michel** – PI, Incubator Group<br><br>**Dr. Jacques Zimmer** – PI, Incubator Group |
| 15:15 – 15:30 | Tea/coffee | |
| 15:30 – 17:15 | Presentation and discussion on research theme 2 'Environment and Immunity/Allergy', based on max. 40 min. short presentations<br><br>15:30 – 15:40<br>Intestinal microbiome and mucosal barrier function<br>**Prof. Mahesh Desai** – PI, Eco-Immunology and Microbiome Group<br><br>15:40-15:50<br>Epigenetics and Early life adversity<br>**Dr. Jonathan Turner** – PI, Epigenetics and Behavioral Immunology Group, Deputy Chair, Finance & Funding<br><br>15:50-16:00<br>Overview on allergy research at DII<br>**Prof. Dr. Markus Ollert** – Director, Department of Infection and Immunity and PI, Molecular and Clinical Allergology<br><br>16:00-16:10<br>Allergen molecules: from diagnostic markers to players in pathogenic mechanisms<br>**Dr. Annette Kuehn** – PI, Molecular and Clinical Allergology<br>**Dr. Christiane Hilger** – PI, Molecular and Clinical Allergology<br><br>16:10 - 17:15 General Discussion | **In presence of:**<br><br>**Prof. Mahesh Desai** – PI, Eco-Immunology and Microbiome Group<br><br>**Dr. Jonathan Turner** – PI, Epigenetics and Behavioral Immunology Group, Deputy Chair, Finance & Funding<br><br>**Prof. Dr. Markus Ollert** – Director, DII and PI, Molecular and Clinical Allergology<br><br>**Dr. Annette Kuehn** – PI, Molecular and Clinical Allergology<br>**Dr. Christiane Hilger** – PI, Molecular and Clinical Allergology |
| 17:15 – 17:30 | Tea/coffee<br><br>17:15-17:25: Client phone call with Dr. Christian O. Simon, Head Medical Affairs,Global Medical and Scientific Affairs Roche Molecular Diagnostics (RMD). | |
| 17:30 – 18:30 | Informal group meeting (with e.g. PhD students or trainees) | PhD Students:<br><br>**Max Meyrath** (Immunopharmacology and Interactomics Group)<br>**Philipp Adams** (LUCID)<br>**Rafaëla Schober** (LUCID)<br>**Christophe Capelle** (Immune Systems Biology Group)<br>**Lynn Bonetti** (Experimental and Molecular Immunology Group) |

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| | | **Luana Guerra** (Experimental and Molecular Immunology Group)<br>**Bente Janssen-Weets** (Molecular and Clinical Allergology)<br><br>Postdocs:<br><br>**Dr Mathieu Amand** (LUCID)<br>**Dr Melanie Grusdat** (Experimental and Molecular Immunology Group)<br>**Dr Martyna Szpakowska** (Immunopharmacology and Interactomics Group) |
| 18:30 – 19:00 | Draft conclusion of the first day | Peers only |
| 19:00 – 20:00 | Transfer to hotel, free time | |
| 20:00 | Dinner | In presence of institute and department management and deputy chairs<br><br>**U. Nehrbass,**<br>**M. Ollert,**<br>**D. Brenner,**<br>**C. Devaux,**<br>**A. Chevigné,**<br>**C. Hilger,**<br>**J. Turner.**<br><br>At Beeftro Belval |

Day 2 – September 20

| Time | Programme | By |
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| 08:15 – 08:45 | Transfer to institute: rue Henri Koch, 29, Esch-sur-Alzette | |
| 08:45 – 10:30 | Presentation and discussion on research theme 3 'Novel structures, topics and platforms' based on max. 40 min. short presentations<br><br>8:45 – 8:55<br>Luxembourg Center for Infectious Diseases (LUCID) – Part 1<br>**Dr. Carole Devaux** – PI, LUCID, Deputy Chair, Quality and Safety<br><br>8.55 - 9:05<br>Luxembourg Center for Infectious Diseases (LUCID) – Part 2<br>**Dr. Judith Hübschen** – PI, LUCID<br><br>9:05 - 9:15<br>National Cytometry Facility (NCP)<br>**Dr. Coralie Guerin** – Head of NCP (until 15th of August 2018)<br><br>9.15 - 9:25<br>CLINNOVA: CoE in digital health and personalized medicine<br>**Prof. Dr. Markus Ollert** – Director, DII, PI, Molecular and Clinical Allergology, LIH initiator and PI, Clinnova<br><br>9:25 - 10:30 General Discussion<br>All scientists present | In presence of :<br><br>**Dr. Carole Devaux** – PI, LUCID, Deputy Chair, Quality and Safety<br><br>**Dr. Judith Hübschen** – PI, LUCID<br><br>**Dr. Coralie Guerin** – Head of NCP (until 15th of August 2018)<br><br>**Prof. Dr. Markus Ollert** – Director, DII, PI, Molecular and Clinical Allergology, LIH initiator and PI, Clinnova |
| 10:30 – 10:45 | Tea/Coffee | |
| 10:45 – 11:45 | Time scheduled for meeting clients/partners of the department<br>10:45-10:55: Client Skype call with Claude Jentgen, Head of Development Cooperation Office in Vientiane, Laos. | 5-10 clients/partners of the department |

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| | MSAN : Mr Patrick Hoffmann (10:55-11:05)<br>UL-LCSB : Dr Regina Becker (11:05-11:15)<br>UL-Animal Facility: Dr Djalil Coowar (11:15-11:25)<br>CHL : Mrs V. Giarmana (11 :25-11 :35)<br>Laboratoires Réunis: 11 :35-11 :45 Client phone call with Prof. Dr. med. Bernard Weber, Director Innovation Unit | |
| 11:45 – 12:15 | Time reserved for clarification of questions from the peers | Department management<br><br>**Prof. Markus Ollert** |
| 12:15 – 13:15 | (simple) Lunch | Peers |
| 13:15 – 14:45 | Time to draft preliminary conclusions | Peers |
| 14:45 – 15:00 | Tea/coffee | |
| 15:00 – 16:00 | Presentation of preliminary conclusions and discussion on possible recommendations | to the department and institute management, client (MESR) and others where relevant |
| 16:00 | End of programme, transfer to train station/airport | |

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