

LIEN - Laboratoire sur les interactions épithéliums - neurones

Rapport Hcéres

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HCERES

High Council for the Evaluation of Research
and Higher Education

Research units

HCERES report on research unit:
Laboratory for Epithelial-Neural Interaction
LIEN

Under the supervision of
the following institutions
and research bodies:

Université de Bretagne Occidentale - UBO

HCERES

High Council for the Evaluation of Research
and Higher Education

Research units

In the name of HCERES,¹

Michel COSNARD, president

In the name of the experts committee,²

Ralf PAUS, chairman of the committee

Under the decree N°2014-1365 dated 14 november 2014,

¹ The president of HCERES "countersigns the evaluation reports set up by the experts committees and signed by their chairman." (Article 8, paragraph 5)

² The evaluation reports "are signed by the chairman of the expert committee". (Article 11, paragraph 2)

Evaluation report

This report is the sole result of evaluation by the expert committee, the composition of which is specified below.

The assessments contained herein are the expression of an independent and collegial reviewing by the committee.

Unit name: Laboratory for Epithelial-Neural Interaction

Unit acronym: LIEN

Label requested: EA

Current number: 4685

**Name of Director
(2015-2016):** Mr LAURENT MISERY

**Name of Project Leader
(2017-2021):** Mr LAURENT MISERY

Expert committee members

Chair: Mr Ralf PAUS, University of Manchester, Manchester, United-Kingdom

Experts: Mr Sélim ARACTINGI, Université Paris Descartes, INSERM (representative of the CNU)
Mr Jérôme LAMARTINE, Université Claude Bernard Lyon 1, CNRS

Scientific delegate representing the HCERES:
Mr Jean-Marie ZAJAC

Representative of supervising institutions and bodies:
Mr Rémi BRAJEUL, University Hospital
Mr Pascal GENTE, University of Bretagne Occidentale

Head of Doctoral School:
Mr Christian BROSSEAU, Doctoral School n° 373, SICMA

1 • Introduction

History and geographical location of the unit

The “Laboratoire des Neurosciences de Brest, LNB”, EA 4685, was created in 2012 and grouped clinicians and scientists from skin, pathology, neurosurgery, neurology, biochemistry. The scientific themes focused on pruritus mainly but also on cancer, glioblastoma, and autism. The previous AERES committee suggested to the group to focus on nerves and skin. For the next contract, a new acronym, LIEN, for Laboratory for Epithelial-Neural Interaction, is proposed. The laboratory is located at the faculty of medicine of Brest in close proximity to clinical departments of the clinicians of the unit.

Management team

The laboratory of Neuroscience de Brest is a single-team unit headed by Mr Laurent MISERY, assisted by a deputy-director, Mr Jean-Luc CARRÉ, elected for 5 years by the general assembly of all lab members.

HCERES nomenclature

SVE, SVE1, SVE1_LS2

Scientific domains

Genetics, functional genomics, biotechnology

Unit workforce

| Unit workforce | Number on 30/06/2015 | Number on 01/01/2017 |
|---|----------------------|----------------------|
| N1: Permanent professors and similar positions | 11 | 15 |
| N2: Permanent researchers from Institutions and similar positions | | 1 |
| N3: Other permanent staff (technicians and administrative personnel) | 1 | 1 |
| N4: Other professors (Emeritus Professor, on-contract Professor, etc.) | 1 | |
| N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.) | 9 | |
| N6: Other contractual staff (technicians and administrative personnel) | | |
| N7: PhD students | 10 | |
| TOTAL N1 to N7 | 32 | |
| Qualified research supervisors (HDR) or similar positions | 7 | |

| Unit record | From 01/01/2010 to 30/06/2015 |
|---|-------------------------------|
| PhD theses defended | 4 |
| Postdoctoral scientists having spent at least 12 months in the unit | 5 |
| Number of Research Supervisor Qualifications (HDR) obtained during the period | 3 |

2 • Overall assessment of the unit

Introduction

The Laboratoire des Neurosciences de Brest (LNB) is focused on pathological perceptions (the way our body senses its environment during the course of a disease) by a combination of approaches including cell biology, pharmacology, physiology, epidemiology or ethology in the field of skin biology and neuroscience. During these last 5 years, the research activities of LNB were divided into several complementary axes including:

Studies of interaction between human skin and the sensory nervous system by co-cultures of sensory neurons with keratinocyte or intact human skin (in skin organ culture).

Epidemiological and histopathological studies of conditions with sensitive skin and/or pruritus.

Study of the mechanisms of pruritus and pain perception, geared toward the development of novel pharmacological treatment strategies.

Study of the psychological aspects of skin disorders and autism, including the role of chloride channels and their inhibition by bupropion.

Studies on the pathophysiology of cancers, including Merkel Cell carcinoma and glioma, had been part of the initial objectives of the LNB but were progressively dropped as had been recommended, even though some members of the lab remained involved in some collaborative studies on this topic during the last years.

Global assessment of the unit

The present application is a renewal of a single-team unit entitled Laboratoire des Neurosciences de Brest (LNB) since its creation in 2012. The unit requests a new name, Laboratoire des Interactions Epithélium Neurone (LIEN), for the next contract. This new name describes nicely the original and unique scientific position of the unit at a biologically, clinically, and commercially very important but underserved research frontier that intimately links dermatology and neuroscience.

The unit exemplarily brings together researchers with multiple and complementary expertise, which are united by a joint focus on pruritus. This model interdisciplinarity is one of the major strengths of the unit, which is on a strong upwards trajectory towards impacting the course of research in its chosen field at the international level. With its focus on pruritus, the unit is well prepared to become one of the very few internationally recognized center of excellence on this topic. However, this will require committed institutional support, namely by the recruitment of additional full-time researchers.

The research projects of the LNB have been very successful during the last years, with important, novel findings leading to a better understanding of the interaction between neural and epithelial cells in human skin and a better management of irritant/sensitive skin. The members of the unit have published very satisfactorily and frequently, with emphasis on publications in leading skin research journals, and have thus increased the international visibility of the unit steadily. They have even been able to obtain recently very innovative, as yet unpublished results, concerning the novel ways how neurons interact with human keratinocytes. The unit members also have raised very substantial financial support both from foundations and from industry, including major global players in the industry that targets skin.

Strengths and opportunities in the context

The unit represents a unique gathering of expertise in multiple and complementary skills from basic to clinical research, from dermatology to neuroscience, from bench to social sciences that is not found elsewhere in pruritus research worldwide. This genuine interdisciplinarity permits a level of global comprehension of pruritus and the addressing of complex, fundamentally and translationally important biological questions in this area that the few existing competing major pruritus groups (USA, Ireland, Germany) are challenged to rival.

It deserves special emphasis that, within Europe, the LNB arguably now holds the leading role among those dermatologically focused pruritus research units, which combine excellent clinical research (incl. trials) with first-rate lab research, not the least due to its landmark human skin reinnervation and neuron-keratinocyte interaction assays.

Worldwide, the LNB is one of the very few centers devoted to the underserved and under-researched, but both clinically and commercially highly relevant, areas of pruritus, neurodermatology, and psychodermatology - all the field of dermatology awaiting the development of more satisfactory therapies. Given that chronic pruritus is one of the most debilitating symptoms in all of clinical medicine, the LNB fills a major gap in translational biomedical research and addresses an unmet, major health care challenge. That the unit does this with a strictly interdisciplinary strategy and at a high level of creativity and innovation puts the LNB in an excellent position to influence where these fields are moving on an international level. The LNB is very well positioned to realize translational research, better than other competing European institutions which are focused on basic research in neurophysiology and neuroimmunology of itch.

The LNB has demonstrated a very good to excellent scientific publication output, especially in clinical research. Namely, the LNB's review published in Nat Rev Neurol documents the rapidly growing international reputation it has acquired in neuropathic pruritus research over the last years.

Given that major studies in the field typically take 3-5 years from initiation to publication, it is to be expected that this relatively young unit does not yet have many first and/or senior author publications in top journals. Moreover, the expert committee was impressed by very exciting, as yet unpublished, data generated within the unit (e.g., demonstration of a keratinocyte-neuronal synapsis), which promises to lead to a landmark publication within the near future and to change currently dominant research paradigms in pruritus research.

The unit has built impressive national and international collaboration networks and has managed to achieve recognition as a key research center, center of reference, and resource center in the field of human skin neuroscience and pruritus research.

Given that, over the past decade, funding support for translational skin research increasingly came from industry, the LNB's excellent funding record from industry sources must be considered an important strength of the unit, since this will greatly facilitate the unit's capacity to become a magnet for industry studies in human skin neurosciences and pruritus research.

The unit has documented a strong involvement in teaching and in the management of research education and is committed to the public diffusion of scientific culture.

The LNB's national and international reputation is attested by the organization of several large-audience congresses and many invitations of the unit's leader to lectures both nationally and internationally (European Society for Dermatological Research, American Academy of Dermatology).

Weaknesses and threats in the context

The unit has an insufficient number of full time-researchers and harbours several members with precarious employment status.

The unit has a low number of original research paper with a first- and/or senior author in the first skin research journal.

In contrast with its impressive list of industry contracts, the number of patents that have been filed is still relatively low.

Currently, the laboratory is mainly based on, and supported by, the leadership and scientific recognition of its director. The emergence of other leaders from within its ranks needs to be systematically encouraged and fostered.

The relative geographic isolation from other research centers in the west of France renders scientific interactions and collaborations somewhat more difficult than elsewhere. This requires greater efforts to connect the unit to its field at both the national and international level, and to make it an attractive work place also for students and scientists beyond the region.

The unit has only few international students, scientists and visitors or invited speakers and conducts its daily operation exclusively in French, thus limiting accessibility and attractiveness beyond France.

Recommendations

The expert committee views the unit as having a strong potential for becoming a credible candidate for application for INSERM status on the next evaluation. However, this requires constant support on its successful upwards trajectory from the university and the hospital. The unit should propose clear strategies for recruiting researchers in the next years: this should also parallel a higher ratio of scientists/MD in the group.

These new full-time researchers should then fully focus on the two areas where the unit the committee feels the unit has its greatest strengths: in-depth study of the keratinocyte-neurons synapse(s), and further development and characterization of *ex vivo*-reinnervated, organ-cultured human skin.

As industry funding is notoriously unpredictable and does not always favour the generation and timely publication of top-level science and/or ambitious long-term projects, the unit would be well-advised to broaden its funding base at least somewhat, namely so as to include French and European public or charitable organisms (ANR, FRM,...).

The expert committee recommends that the clinicians in the unit are granted a higher percentage of their work time that is dedicated exclusively to research, and pertains that only those clinicians can realistically be expected to contribute significantly to the unit's research output who can devote 50% of their time to pruritus-related research.

The unit should work to systematically promote the emergence of at least one additional senior scientist and one clinician who become internationally recognized in the fields of human skin neuroscience and pruritus, to assist the director in publicizing and promoting the unit's mission, achievement, and scientific appeal, and to gradually build an independent career in this specific field of research, also for facilitating an eventual handover in due course. The internal scientific life of the unit should be further vitalized and internationalized, e.g. by extending journal club activities held in English and organizing more seminars with external invited speakers.

The unit should place greater emphasis on publishing every year a first- and/or senior author original research paper in the #1 skin research journal (*J Invest Dermatol*), in favour of reducing its quantitative output in minor journals. This will further strengthen its international visibility & leadership within the skin research community, namely in human skin neuroscience and pruritus research.

The LNB's range of funding sources should be broadened so as to go beyond the private sector and should also target government, E.U., and foundation sources. In the E.U. funding context, it should be possible to forge strategic research alliances with other key pruritus research centers (e.g. Dublin, Münster, Mannheim), e.g. by offering the unit's skin reinnervation and keratinocyte-neuron interaction models to collaborating external investigators.