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Le système nerveux entérique dans les maladies de l'intestin et du cerveau

Rapport Hcéres

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HCERES

High Council for the Evaluation of Research
and Higher Education

Research units

HCERES report on research unit:

Neuropathies of the enteric nervous system and
digestive pathologies: implication of enteric glial cells

Under the supervision of the following
institutions and research bodies:

Université de Nantes

Institut National de la Santé Et de la Recherche
Médicale - INSERM

Evaluation Campaign 2015-2016 (Group B)

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

Eva EKBLAD, chairwoman of the committee

Under the decree N^o.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: Neuropathies of the enteric nervous system and digestive pathologies:
implication of enteric glial cells

Unit acronym:

Label requested: UMR

Current number: 913

**Name of Director
(2015-2016):** Mr Michel NEUNLIST

**Name of Project Leader
(2017-2021):** Mr Michel NEUNLIST

Expert committee members

Chair Ms Eva EKBLAD, Lund University, Lund, Sweden

Experts: Mr Pascal de SANTA BARBARA, Université de Montpellier (representative Inserm CSS)

Mr Karl-Herbert SCHÄFER, University of Applied Sciences Kaiserslautern Campus
Zweibrücken, Germany

Scientific delegate representing the HCERES:

Mr Jacques NOËL

Representatives of supervising institutions and bodies:

Mr Frédéric BENHAMOU, Université de Nantes

Ms Meriem MAROUF-YORGOV, Inserm

Ms Anne-CLaire de REBOUL, CHU of Nantes

Head of Doctoral School

Ms Corinne MIRAL, Doctoral school ED n° 502 "Biologie Santé"

1 • Introduction

History and geographical location of the unit

The UMR 913 unit was formed in 2008 as a mono-team unit dealing with the concept of studying intestinal neuro-glio-epithelial interactions in health and disease. It was renewed in 2012. The unit is part of the “Institut des Maladies de l’Appareil Digestif” (IMAD) of the University Hospital of Nantes and a founder member of the “Département Hospitalo-Universitaire” (DHU2020). It is strategically localised in close contact with the University Hospital of Nantes and Nantes University. Such an environment strongly promotes translational research, which has been a key work model within the unit. The unit also has ongoing collaborations with industry.

The unit has expanded in recent years. The number of employees, staff as well as researchers, has increased, as has the number of subprojects. The translational approach is made possible not only by the close geographic connection with the Hospital, but also due to a strategic decision to involve both clinical and basic researchers in scientific and training programs as well as by the creation of technical platforms.

Management team

The unit is headed by its founder Mr Michel NEUNLIST.

HCERES nomenclature

SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie

SVE1_LS5 Neurosciences

SVE1_LS7 Recherche clinique, Santé publique

Scientific domains

The unit conduct translational research in Neurogastroenterology aiming at a better understanding of underlying mechanisms of several diseases with particular focus on gastrointestinal entities. Also the connection between enteric end central nervous disease mechanisms is addressed. Biomarkers and therapeutic alternatives for human diseases like inflammatory bowel disease (IBD), colorectal cancer and other chronic diseases are sought. Underlying disease mechanisms are studied in various animal models constantly refined and developed.

Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	5	8
N2: Permanent researchers from Institutions and similar positions	6	6
N3: Other permanent staff (technicians and administrative personnel)	5	5
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	4	
N6: Other contractual staff (technicians and administrative personnel)	6	
N7: PhD students	14	
TOTAL N1 to N7	40	
Qualified research supervisors (HDR) or similar positions	7	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	11
Postdoctoral scientistshaving spent at least 12 months in the unit	4
Number of Research Supervisor Qualifications (HDR) obtained during the period	5

2 • Overall assessment of the unit

Introduction

The main focus of the unit is to characterise various aspects of the concept of the neuro-glio-epithelial unit (NGEU). This includes carrying out clinical as well as basic research on the role of the enteric nervous system, including enteric glia, and in chronic intestinal diseases, but also to characterise NGEU dysfunctions in Parkinson's disease. Intestinal inflammation and the intestinal epithelial barrier (IEB) are of central interest to the unit. Enteric glia is found to be of importance for IEB repair, and several mediators, in particular n-6 derived lipids, are presently studied. Further, neurostimulation as a therapeutic option to restore IEB homeostasis has been suggested and these aspects are currently investigated.

The involvement of NGEU, as well as microbiota, during obesity, tumorigenesis and development is addressed with the aim of improving therapeutic handling and finding biomarkers.

In Parkinson's disease, co-morbidity in the NGEU forms the basis to further study the NGEU as a source of biomarkers to evaluate disease progression and severity.

Since previous evaluation (in 2011) the scope of diseases and neuropathies investigated by the unit has significantly been broadened. The number of subprojects has markedly increased. Several new aspects on the possible role of NGEU in intestinal as well as central diseases are described and explored.

Global assessment of the unit

The close connection of the unit with hospital and university fosters translational research. The unit has an internationally leading position in Neurogastroenterology. It is well funded, from internal as well as external sources, and active in recruiting both clinical and basic science researchers and PhD students. The research profile is unique, innovative and translational and has fostered scientific collaborations in national and international networks as well as with industry. The unit is well organised concerning technical platforms, expertise, equipment, facilities and infrastructure. Internal and external communication is well structured. The unit is actively involved in basic education, public outreach and in several national and international scientific networks. The unit increased its interaction with the public significantly during the last years (national TV, press media and radio). The unit is very successful in raising internal and external funds. The funding has increased by 33% during the five-year period, in particular concerning private and public funding.

Strengths and opportunities in the context

The unit holds 4 patents. The expansion of the unit has led to the development of new experimental models and new therapeutic concepts. The unit has participated in 4 clinical trials. Scientific output is high and internationally recognised. The NGEU/IBD project is highly interesting, focussing on neuroimmune interactions, and has good chances to develop prognostic tools or to identify biomarkers to favour therapeutic progress. The NGEU/colorectal cancer project is highly original and might conduct to the identification of new molecular mechanisms essential for homeostasis. The NGEU/Parkinson project has a high international visibility and attracts funding.

Weaknesses and threats in the context

The expansion of the unit challenges the basic organisation of the unit (e.g. integration and incorporation of new staff and students). Recruitment of new PhD students, in particular from abroad, is reported difficult. There is a high risk that the increasing number of subprojects will be difficult to handle and cause fragmentation of the organisation and loss of scientific focus. This is of particular concern in the NGEU/neurodevelopment and neurodegeneration project, in which the studies on 4 different ENS and CNS (central nervous system) neurological diseases are interesting, but require different expertise in paediatric and adult fields, which threatens to dilute task forces. Also the NGEU/IBS project is very ambitious but in need of a strong immunological input. The value of DSS (Dodecyl Sodium Sulphate) and TNB (Trinitro Benzene sulfonic acid) models for this latter study is debatable. The project on NGEU and carcinogenesis is internationally very competitive, but recruitment of scientists to reinforce basic science approaches would markedly increase feasibility.

Recommendations

The main concern for the unit is the number of subprojects: there is an impressive number of subprojects reported in the program, but the feasibility is questionable in the current setting. There is a risk for superficial studies, generating several publications but not in depth studies, and thus harder to publish in high impact journals. The unit should emphasis quality rather than quantity.

The recruitment of, or the collaboration with, an immunologist in the IBD project would increase the strength of the project. Further, in the IBS project, the animal models should be evaluated concerning their appropriateness and the inclusion of additional models should be considered.

In the colorectal cancer project the influence of ENS on different digestive cancer types, such as colorectal and gastric, should be clearly examined and compared. Influence of other components in the microenvironment, such as myofibroblasts and vasculature, should be considered in order to obtain a complete map.

The project “neurodevelopment and neurodegeneration” would benefit if focused mainly on neurodegenerative diseases in order to further strengthen its international position.

The nutritional and microbiome aspects are rather underrepresented and do not really fit in the context of all other approaches. It could either be a topic of its own or dropped. The pig model, in case of delivering an appropriate immune response, could be used in the IBS project.

Recruitment of foreign PhD students and researchers should be intensified.