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# PHIND - Physiopathologie et imagerie des troubles neurologiques

Rapport Hcéres

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# HCERES

High Council for the Evaluation of Research  
and Higher Education

Research units

HCERES report on research unit:

Physiopathology and Imaging of Neurological Disorders

PhIND

Under the supervision of the following  
institutions and research bodies:

Université de Caen Basse-Normandie - UCBN

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

Établissement Français du Sang - EFS

# HCERES

High Council for the Evaluation of Research  
and Higher Education

Research units

*In the name of HCERES,<sup>1</sup>*

Michel COSNARD, president

*In the name of the experts committee,<sup>2</sup>*

Rick DIJKHUIZEN, chairman of the committee

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

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

<sup>2</sup> 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:	Physiopathology and Imaging of Neurological Disorders (Former name: Serine Proteases and Pathophysiology of the Neurovascular Unit)
Unit acronym:	PhIND (Former: SP2U)
Label requested:	UMR-S INSERM / Univ. Caen / EFS
Current number:	UMR-S U919
Name of Director (2015-2016):	Mr Denis VIVIEN
Name of Project Leader (2017-2021):	Mr Denis VIVIEN

## Expert committee members

Chair:	Mr Rick DIJKHUIZEN, University Medical Center Utrecht, the Netherlands
Experts:	Mr Gilles BONVENTO, CEA, Fontenay aux Roses Ms Jöelle CHABRY, Institut de Pharmacologie Moléculaire et Cellulaire, Sophia Antipolis, Nice (representative of the INSERM) Mr Florian LESAGE, IPMC, Sophia Antipolis, Nice (representative of the CNU)
Scientific delegate representing the HCERES:	Mr Jean-Marie ZAJAC
Representatives of supervising institutions and bodies:	Ms Chantal LASSERVE, INSERM Mr Guy LAUNOY, University of Caen Mr Frederick MARIE, Caen University Hospital Mr Samir OULD-ALI, INSERM Mr Jean Christophe PAGES, EFS
Head of Doctoral School:	Mr François DAUPHIN, Doctoral school n° 497, ED NBISE

## 1 • Introduction

### History and geographical location of the unit

The proposed tripartite unit “Physiopathology and Imaging of Neurological Disorders” (PhIND) is a follow-up of the INSERM mono-team research unit 919 (UMR-S U919), entitled ‘tPA in the working brain’, created in 2008 under the responsibility of Mr Denis VIVIEN, which was renewed and renamed in 2012 as “Serine Proteases and Physiopathology of the neurovascular Unit (SP2U)” with the same director.

The unit is hosted by the “Groupement d’intérêt publique” (GIP) Cyceron (Campus Jules Horowitz), in Caen, which offers a platform for investigations from molecular to integrated levels, through access to equipments of the GIS-IBISA platform for in vivo imaging (7T and 3T Magnetic resonance imaging, near infrared fluorescence, confocal imaging - in U919, multiphoton microscopy) and to a recently built animal facility (University of Caen).

### Management team

The unit is headed by Mr Denis VIVIEN.

PhIND consists of three teams. Team A: tPA and Neurovascular Disorders, is headed by Mr Denis VIVIEN, Team B: Serine Proteases, Neuroinflammation and Glial cells, is headed by Mr Fabian DOCAGNE, Team C: Multimodal Neuroimaging and Lifestyle in Ageing and Alzheimer’s Disease, is headed by Mr Gaël CHETELAT.

### HCERES nomenclature

SVE1\_LS5 Neurobiologie

SVE1\_LS7 Epidémiologie, santé publique, recherche clinique, technologies biomédicales

### Scientific domains

Molecular biology, cell biology, in vivo imaging, neuroscience

## Unit workforce

Unit workforce	Number on 30/06/2015	Number on 01/01/2017
N1: Permanent professors and similar positions	13	17
N2: Permanent researchers from Institutions and similar positions	2	3
N3: Other permanent staff (technicians and administrative personnel)	7	9
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	7	
N6: Other contractual staff (technicians and administrative personnel)	1	
N7: PhD students	23	
<b>TOTAL N1 to N7</b>	<b>53</b>	
Qualified research supervisors (HDR) or similar positions	14	

Unit record	From 01/01/2010 to 30/06/2015
PhD theses defended	17
Postdoctoral scientists having spent at least 12 months in the unit	8
Number of Research Supervisor Qualifications (HDR) obtained during the period	4

## 2 • Overall assessment of the unit

### Introduction

PhIND aims at developing and applying innovative research methods, focused on molecular biology, cell biology, physiology, behaviour and brain imaging, to elucidate mechanisms underlying functions and dysfunctions of the central nervous system, with a special interest on serine proteases (especially tPA), inflammatory processes and ageing. The unit promotes a translational approach with close interaction between basic research and clinical practice.

Currently, the UMR-S U919 is a mono-team unit, which has been focusing on translational research on neuroprotective and/or pro-fibrinolytic strategies in stroke, inflammatory processes and age-related brain-dysfunctions. There has been a strong interest in the development and application of brain imaging tools, which has been reinforced when Mr Gaël CHÉTELAT (ex INSERM UMR-S U1077) joined the unit in 2015.

### Global assessment of the unit

The future unit will be constituted of three research teams that aim at elucidating physiopathological mechanisms of neurological disorders and at developing diagnostic tools and therapeutic strategies that could ultimately lead to improved outcome for patients. The research program has a specific focus on serine proteases (particularly tPA), and involves a powerful translational approach, with a central role for imaging techniques. The team leaders are internationally renowned scientists in the fields of molecular neurobiology in cerebrovascular and neuroinflammatory disorders (Teams A and B) or neuroimaging in Alzheimer's disease (Team C). They have a very impressive track record in terms of scientific output and technology transfer of their research findings. Furthermore, they have been highly successful in raising local, national and international funding.

The well-managed unit benefits from a well-equipped infrastructure for multidisciplinary studies and a close link with clinicians, which provides an excellent basis for bench-to bedside-to-bench studies ranging from basic science to (pre)clinical research. Their organization also offers excellent internal PhD training opportunities. The teams have proposed an original, ambitious and promising five-year plan, which builds upon their previous successful achievements and includes novel strategies that can effectively benefit from interaction between the three teams.

### Strengths and opportunities in the context

The scientific scope, achievements and outputs, as measured from publications and invited lectures, are excellent to outstanding, both qualitatively and quantitatively according to international standards. The unit consists of talented and ambitious team leaders, with a good balance between early-career and established scientists, who have developed and applied original and pioneering research approaches ranging from basic science to clinical studies. This will be extended in the proposed five-year plan with a highly promising and original research program focused on neurological disorders, particularly stroke, multiple sclerosis (MS) and Alzheimer's disease.

The leaders of Team A (unit director) and Team C are internationally recognized experts in the fields of protease and neurobiology (Team A) and neuroimaging of Alzheimer's disease (Team C). Team B is an emerging group with original concepts for research in the field of MS. The team leaders have been very successful in raising local, national and international funds, which provides an important basis for their successful achievements.

The composition of the unit and of the teams, which include clinicians, offers a very strong potential for efficient translational research, for example through use of neuroimaging tools that are available in experimental and pre-clinical settings. Furthermore, various successful partnerships with academic and non-academic institutions (locally, nationally and internationally) provide excellent opportunities for transfer and translation of their scientific results.

The unit is very well managed with a unique infrastructure for multidisciplinary studies and excellent training opportunities for PhD students.

### Weaknesses and threats in the context

The wide extent of the research projects may carry a risk of over ambition at the expense of scientific focus, particularly for the single permanent researcher in Team B. This may be further threatened by shortage of technical support. Optimal clinical translation might be confined by the absence of clinicians as principal investigators in some of the teams.

Despite the great potential for a powerful joint translational research program, the exact strategy for continuing interaction between the three teams on the long-term is not fully clear. In particular, the integration of the program of Team C into the more basic science programs of Teams A and B requires attention.

There are only a few international PhD students or post-docs in the teams.

Although internal PhD training is excellent, the participation of PhD students in the doctoral school program is at a low level.

### Recommendations

Further collaborative studies should be developed, particularly for Team C with Teams A and B, in order to promote the integration of Team C in the new unit.

Team B should keep focusing on MS, and the team leader needs to be supported in his development to become an independent principal investigator, for example through senior authorships on publications. This team should also aim at financial independence by increasing the part of its own grants.

Translational approaches can be strengthened by more involvement of clinicians at all levels of the scientific programs, i.e. from basic science to clinical applications.

Technical support and expertise should be increased, for example for electrophysiology and in vivo animal experimentation studies.

More foreign students and post-docs should be attracted.

Possibilities to improve the participation of the unit in the doctoral school program should be discussed between the director of the unit and the doctoral school.