FINAL RESUME ON THE RESEARCH UNIT
GPMCND - Génomique et médecine personnalisée du cancer et des maladies neuropsychiatriques

UNDER THE SUPERVISION OF THE FOLLOWING INSTITUTIONS AND RESEARCH BODIES:
Université de Rouen
Institut national de la santé et de la recherche médicale - INSERM

EVALUATION CAMPAIGN 2020-2021
GROUP B

Report published on September, 23 2021
Under the decree No.2014-1365 dated 14 November 2014,

1 The president of Hcéres “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 experts committee”. (Article 11, paragraph 2)
UNIT PRESENTATION

Unit name:  
GPMCND - Génomique et médecine personnalisée du cancer et des maladies neuropsychiatriques  

Unit acronym:  
GPMCND  

Current label and N°:  
U1245  

ID RNSR:  
201722543J  

Application type:  
Renewal  

Head of the unit (2020-2021):  
Mr Thierry Frebourg  

Project leader (2021-2025):  
Mr Gaël Nicolas  

Number of teams and/or themes:  
5

EXPERTS COMMITTEE MEMBERS

Chair:  
Mr Stanislas Lyonnet, Université de Paris

Experts:  
Ms Karine Bertaux, Hopitaux Universitaire de Marseille, APHM  
Mr Gabriel Capella, IDIBELL, Bellvitge Biomedical Research Institute, Espagne  
Ms Geneviève Gourdon, INSERM Paris  
Mr Stanislas Lyonnet, Université de Paris  
Ms Fanny Mochel, INSERM Paris  
Ms Simone Niciou, Luxembourg Institute of Health, Luxembourg  
Ms Jessica Zucman-Rossi, INSERM Paris

HCÉRES REPRESENTATIVE

Mr Yacine Graba

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Ms Annie Gaumont, Université Caen  
Mr Etienne Hirsh, INSERM  
Ms Catherine Nguyen, ITMO  
Mr Samir Ould-Ali, INSERM  
Mr Vincent Richard, Université Rouen
INTRODUCTION

HISTORY AND GEOGRAPHICAL LOCATION OF THE UNIT

The UMR U1245 unit (INSERM and University of Rouen) was created by Mr Thierry Frebourg in January 2017 with four groups: two teams already led by Mr Frebourg and Mr Dominique Campion, respectively (both created in 2011), a unit on lymphoid neoplasms directed by Mr Fabrice Jardin, and an ERI from INSERM on neonatal brain lesions and microvascular endothelium directed by Mr Bruno Gonzalez.

The merger of this new large centre corresponding to the four founding teams now includes a fifth group originating from the INSERM U1239 unit working on the genetic characterization of brain tumours and their therapeutic targets. This set of successive mergers resulted in a very large multi-team research unit (5 teams) sharing the following general characteristics: all depend on INSERM and the University of Rouen and have a research field in genetics and genomics; there is a general consistency of fundamental and very translational research work in the neurodevelopmental, cerebral, somatic and constitutional oncogenetic fields; all groups are located in the medical faculty of Rouen and on its medical campus, in two floors of the research building of the faculty. Team 2 remains for the moment located very close in the Comprehensive Cancer Centre Henri Becquerel, facing the faculty.

This regrouping shows a remarkable dynamic of genetics and medical genomics at the University of Rouen and INSERM in this context.

The committee must immediately draw attention to the exceptional circumstances with which this Centre was confronted in its evaluation since the project leader, Mr Thierry Frebourg, an internationally renowned geneticist, particularly in oncogenetics and neurogenetics, unfortunately passed away, very suddenly, even though the application had been submitted in March 2021, leaving the whole of this research Centre in a very difficult situation. To say this is also to pay immediate tribute not only to Mr Frebourg, to his work and his great achievements, but also to the exceptional mobilization of the researchers, physician researchers, academics, engineers and technicians, from this important Centre who immediately mobilized to take charge of the project, to assume its governance, and to present it in the best possible way, thus paying an exceptional tribute to Mr Thierry Frebourg and to his vision.

This is what allowed the mixed assessment of this research structure by the HCERES committee:

- first on file, in the pandemic context,
- but also, by requesting a dedicated afternoon of synthetic presentations of the entire program and scientific chapters and projects by each of the five teams, allowing them to express their views in such an unexpected and stressing context.

It is therefore at the end of this very particular process that this report has been written.

RESEARCH ECOSYSTEM

The research unit in its present configuration: « Genomic and Personalized Medicine in Cancer and Neurological disorders » (GPMCND) is deeply embedded in the ecosystem of the Normandie region: above all, the Rouen university hospital campus, its medical school (faculté) and its research building, the Comprehensive Cancer Centre Henri Becquerel in Rouen, located opposite to the medical school, but also, strong links exist with the Comprehensive Cancer Centre of Caen François BACLESSE as well as the CHU of Caen and its university.

Further, the GPMCND unit is a founding member of the Institute for Research in Innovation and Biomedicine (IRIB) of the University of Rouen, a federation that brings together five INSERM units and two CNRS as well as eight university laboratories and the clinical investigation centre.

Likewise, the unit is the hard core of the Normandie Centre for Medical Genomics and Personalized Medicine (NGP) created in 2015 and labelled as a FHU, and managed, until his death, by Mr Thierry Frebourg himself.

The ecosystem in question therefore constitutes a “whole” that makes this federation, centred on the GPMCND unit, not only a regional but also a national and European force of great strength in medical genomics and all the translational activities that may affect it. This involves, in particular, large patient cohorts in the field of cancers (breast cancer, colorectal cancers, hereditary cancers), intellectual disability and related syndromes, genetic forms of Alzheimer’s Disease. This also echoes the links with medical and university hospital genomics and, in particular, the developments in terms of genetic testing by new generation sequences in these same fields (in the order of 6,500 patients tested per year for constitutional DNA and over 3000 annual analyses of tumours).
This clearly shows the importance of the GPMCND unit, the five teams that make it up and their deep integration into a medical genomics ecosystem of which it is clearly the initiator.

HCÉRES NOMENCLATURE AND THEMATICS OF THE UNIT

Main scientific area: SVE; with subdomain SVE5-3, SVE5-4, SVE4-2, SVE2-2.

MANAGEMENT TEAM

In the current configuration, reviewed after the sudden death of Mr Thierry Frebourg, Mr Gaël Nicolas, academic and molecular geneticist, took over the unit direction and will be in charge of the future “Cancer and Brain Genomics” (CBG) unit. Mr Bruno GONZALES is and will remain the deputy director.

UNIT WORKFORCE

Cancer and Brain Genomics

<table>
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<tr>
<th>Active staff</th>
<th>Number 06/01/2020</th>
<th>Number 01/01/2022</th>
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<tr>
<td>Full professors and similar positions</td>
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<td>15</td>
</tr>
<tr>
<td>Assistant professors and similar positions</td>
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<td>18</td>
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<tr>
<td>Full time research directors (Directeurs de recherche) and similar positions</td>
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<td>3</td>
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<tr>
<td>Full time research associates (Chargés de recherche) and similar positions</td>
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<td>3</td>
</tr>
<tr>
<td>Other scientists (“Conservateurs, cadres scientifiques des EPIC, fondations, industries, etc.”)</td>
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<tr>
<td>High school teachers</td>
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<tr>
<td>Supporting personnel (ITAs, BIATSSs and others, notably of EPICs)</td>
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<tr>
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<tr>
<td>Non-permanent supporting personnel</td>
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<td>Non-permanent staff</td>
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<tr>
<td>Total</td>
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<td>91</td>
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GLOBAL ASSESSMENT OF THE UNIT

The Genomic and Personalized Medicine in Cancer and Neurological disorders » (GPMCND) unit to be renamed for the next contract “Cancer and brain genomics” (CBG) at the University of Rouen and with INSERM as co-supervising body, is a very strong structure addressing genetics and genomic mechanisms underlying the emergence of cancer, neurologic, and neuro developmental diseases.
Strengths of the unit build upon a strong cohesion and scientific coherence provided by different contexts: 1/ an undisputable nationwide activity but also a visibility at the international level, particularly in terms of networks, working groups, consortium, particularly for Team 3, and those in the field of cancer and neurogenetic disorders, 2/ a shared philosophy of genomic medicine, emphasizing the close integration between clinical and biology, between care and research, between genomics and good medical practice, particularly in the field of prescription and organization of genetic tests at national and European scales, 3/ an in-depth sharing of a very high-level methodologies in terms of genome sequence, transcriptome, epigenome, gene expression analysis, all based on two high-level genomics platforms from the Universities of Rouen and Caen, 4/ a strong emphasis on the annotation of genomic variants and the use of bioinformatics, in particular for the exploration of non-coding domains of the genome, 5/ the use of up-to-date methods and technologies of functional analysis of variants of unknown significance already in place and under development as well as, in parallel, innovations in the field of statistics, classification of genomic variants, 6/ strong intention to increase discoveries towards medical transfer and in particular the development of new biomarkers, diagnostic tests, prognostic tests, molecular theragnostic tests and, ultimately, 7/ participation in clinical trials in the field of neuroscience and cancer.

The scientific production, judged on the publications is of very good quality, regular, sustained, regularly reaching the level of the best journals of the various specialties but also, often in collaboration, as frequently in these disciplines, of the international general journals of the highest level. This has led to 443 publications for the evaluated period some in high-profile journals including Nucleic Acid Research, Clinical Cancer Research, Molecular Psychiatry, PLOS Medicine. However, the number of high-profile publications is still somewhat insufficient and could be improved. The unit has a high level of national collaborations, and several international, in an extremely competitive context in all fields. The unit has an indisputable visibility in French genetics and genomics landscapes, but also internationally and Team 3 is an international leader in the field of the genetics of AD, and related disorders (tauopathies, cerebral amyloid angiopathy) as outlined by the co-coordination of the ADES European consortium and excellent scientific output.

The fundraising capacity of the unit is mainly at the national level (FHU, ANR, PHRC, INCa-Plan Cancer, ARC and Ligue-Cancer) and would benefit from targeting competitive international (European) grants which are lacking and whose success could improve the unit’s international recognition as a whole.

Non-academic activities are rich, evenly distributed across the teams. In particular, strong links with the national strategies of genetic testing and precision medial genomics have been developed. The patent (6) and invention declaration (4) activities are sustained. A total of five Software suites, three DataBases, and six declared cohorts or BioBanks, have been developed. Combined, those assets in technology transfer should be recognized as excellent. There are in addition solid involvements in international clinical trials, both in Team 2 (new markers for lymphoma and leukemia predictive of response to treatment in the international LYSA group), and neurogenetics in Team 3 (an innovative international prevention trial in Alzheimer, DIAN-TU, directed by Washington University, Saint Louis, USA). Partnerships with industry could however be reinforced as well as technology transfer activities, whenever possible. Another very successful approach, whatever the themes, and one of the great successes of the unit and the teams that make it up, is the constitution of medical cohorts remarkably phenotyped and ready for genomic analyses but also towards clinical trials.

The involvement in academic training is excellent although the number of PhD currently ongoing is low compared to the general dynamic of the unit.

The governance pattern of the CBG, in the line of the previous established governance of the GPMCD is outstanding.

Regarding the scientific proposal for the next contract, the proposed objectives seem excellent, with ambition but measured risks, again in each of the teams. One of the future challenges of the CBG management will in fact be to ensure cross-fertilization between the groups, as the size of the centre is now quite large. Finally, despite its coherence and cohesion, one of the risks inherent in the size of this structure is obviously a possible tendency to dispersion.
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