FINAL RESUME ON THE RESEARCH UNIT
MRGM - Maladies Rares : Génétique et Métabolisme

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

EVALUATION CAMPAIGN 2020-2021
GROUP B

Rapport publié le 20/05/2021

High Council for evaluation of research and higher education
In the name of Hcéres¹:
Mr Thierry Coulhon, President

In the name of the experts committee²:
Mr Stanislas Lyonnet, Chairman of the committee

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:
Maladies Rares : Génétique et Métabolisme

Unit acronym:
MRGM

Current label and N°:
U1211

ID RNSR:
201622185Z

Application type:
Renewal

Head of the unit (2020-2021):
Mr Didier Lacombe

Project leader (2021-2025):
Mr Didier Lacombe

Number of teams and/or themes:
2

EXPERTS COMMITTEE MEMBERS

Chair: Mr Stanislas Lyonnet, Institut Imagine, Université de Paris

Experts:
Ms Barbara Bardoni, IPMC Université Côte d’Azur
Mr Olivier Feron, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium
Ms Corinne Lebreton, Institut Imagine, Université de Paris
Mr Alain Verloes, Hôpital Robert-Debré, Paris
Mr Antonio Zorzano, Complex Metabolic Diseases and Mitochondria, Barcelona, Spain

HCÉRES REPRESENTATIVE

Mr Hinrich Gronemeyer

REPRESENTATIVES OF SUPERVISING INSTITUTIONS AND BODIES

Mr Alain Pierre Gadeau, Université de Bordeaux
Ms Catherine Nguyen, INSERM
Mr Éric Papon, Université de Bordeaux
Mr Richard Salive, INSERM
INTRODUCTION

HISTORY AND GEOGRAPHICAL LOCATION OF THE UNIT

The MRMG (Rare diseases: genetics and metabolism) research unit was created in 2010 as an EA of the Bordeaux University, by merging teams of several previous UMRs. Subsequently, the MRMG obtained the label INSERM unit 1211 (INSERM / University of Bordeaux) for the five-year contract 2016-2020, which was extended to 2021. The current assessment is therefore considered a renewal. MRMG trustees (“tutelles”) are therefore both INSERM and the University of Bordeaux, the latter being now a single university.

Unit 1211 MRMG is mostly located on a single site at the Pellegrin Hospital of the University of Bordeaux on the Carreire campus, a privileged location, close to University hospital activities allowing quality translational activity. However, the ZebraFish platform is still located on the Talence site (ten minutes by car). Discussions are underway for a final regrouping on the campus.

RESEARCH ECOSYSTEM

The unit’s ecosystem is thus, unfortunately still, spread over two sites, although a solution appears tangible and the plans of the University to regroup the Bordeaux campus foster hopes that there may be a single site in the future. However, this perspective seems to be linked to hospital decisions, since the current building is under the supervision of the University hospital. Anyway, apart from the classical partners (University of Bordeaux, IdEx, CHU Pellegrin), the unit is strongly connected with national actions such as the “Plan National Maladies Rares” (version 3), in particular with two labelled “Centres de référence Maladies Rares” (CRMRs), the Plan “France Médecine Génomique” (FMG 20-25), the ITMO “Génétique, Génomique, Bioinformatique”. The MRMG is also a key part of the Bordeaux biomedical ecosystem comprising the NeuroCampus, the SIRIC OncoSphere, the IBGC of CNRS, and the Functional Genomic Center (CGFB).

HCÉRES NOMENCLATURE AND THEMATICS OF THE UNIT

SVE 2

MANAGEMENT TEAM

Since its creation, the MRMG unit has been headed by Mr Didier Lacombe, professor of genetics (CNU 47.04), head of the genetic department of the CHU Pellegrin in Bordeaux. This has resulted in a clearly structured management of the unit, strongly connecting the pre-clinical and clinical research, which is a key issue in the domain of genetic disorders in general, and, in particular, developmental anomalies characterized by a vast range of expression and a broad genetic heterogeneity.

UNIT WORKFORCE

**MRGM - Maladies Rares : Génétique et Métabolisme**

<table>
<thead>
<tr>
<th>Active staff</th>
<th>Number 06/01/2020</th>
<th>Number 01/01/2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full professors and similar positions</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Assistant professors and similar positions</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Full time research directors (Directeurs de recherche) and similar positions</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Full time research associates (Chargés de recherche) and similar positions</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other scientists (&quot;Conservateurs, cadres scientifiques des EPIC, fondations, industries, etc.&quot;)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>High school teachers</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Supporting personnel (ITAs, BIATSSs and others, notably of EPICs)</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td><strong>Permanent staff</strong></td>
<td><strong>28</strong></td>
<td><strong>24</strong></td>
</tr>
</tbody>
</table>
Non-permanent professors and associate professors, including emeritus

Non-permanent full time scientists, including emeritus, post-docs (except PhD students) 5

PhD Students 11

Non-permanent supporting personnel 4

Non-permanent staff 20

Total 48 24

GLOBAL ASSESSMENT OF THE UNIT

The MRGM was formed and presented itself as a single team unit with two different themes: i) genetic anomalies of development, and ii) innate errors of mitochondrial metabolism.

Overall, the unit gives the impression of cohesion, dynamism, sustained supervision of students, whatever the level, and of the general coherence of approaches despite the dispersion that is generally unavoidable in the field of genetic diseases which are often rare and always heterogeneous.

The scientific production judged on the publications is of very good quality, regular and sustained, reaching the good or best journals of the different specialties, such as Human Molecular Genetics or Journal of Investigative Dermatology. The unit also published in high standard or international generalist journals albeit less frequently.

Examples are publications in Nature, Nature Immunology, Journal of Clinical Investigation or Cell Reports.

Despite being administratively a mono-team unit, MRGM is organized along two complementary lines:

- Theme 1 'Genetic Diseases of Development' studies the pathophysiology of rare syndromes: Goldenhar syndrome, Rubinstein-Taybi syndrome, albinism, and RASopathies.

- Theme 2 'Regulation of energy and lipid metabolism' studies the mechanisms of regulation of energy and lipid metabolism. In particular, new actors and drug modulators in this regulation are being sought, notably through the study of rare diseases. It should thus be understood from that viewpoint that both the nature of scientific studies and the publications of Theme 2 are of a more fundamental essence by nature.

Whatever the themes, a major achievement of the unit is the constitution of particularly well-phenotyped cohorts, (mostly mitochondrial and neurodevelopmental disorders, for Theme 2, and developmental anomalies, poly-malformation syndromes, RASopathies, dysmorphic syndromes, etc. for Theme 1) whose biological material is accessible. Another strength is the aim to move forward in the direction of therapies, not only intentionally, but also with tangible results and convincing attempts.

This is why the HCERES site-visit committee has avoided a comparative evaluation of the respective two themes, preferring, on the contrary, to highlight their coherence, their common actions, the spirit of cohesion which they do everything for to reign within the unit. Indeed, although both themes share actions and a similar philosophy in terms of identifying pathophysiological mechanisms in genetic diseases, one cannot compare the approaches available in the field of congenital developmental anomalies (where clinical and genetic heterogeneity reign more than anywhere else), to the approaches implemented for mitochondrial diseases (characterized by particularly developed functional knowledge).

Along these lines, the panel appreciated the ability for important national and international collaborations, as well as an indisputable visibility in the field of French genetics. A recognized and efficient zebrafish platform is an important asset, among other fairly dynamic methodological developments in the unit. Finally, the proximity of University hospital services to the Bordeaux campus is obviously one of the essential elements for the competitive strength of the INSERM 1211 unit.
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