

# Nutrition, diabète et cerveau

Rapport Hcéres

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# High Council for the Evaluation of Research and Higher Education

Research units

# HCERES report on research unit:

Nutrition and the Brain

Under the supervision of the following institutions and research bodies:

Université Claude Bernard Lyon 1 – UCB

Institut National de la Santé Et de la Recherche

Médicale - INSERM



# High Council for the Evaluation of Research and Higher Education

### Research units

In the name of HCERES,1

Didier Houssin, president

In the name of the experts committee,2

Louis Hue, chairman of the committee

Under the decree  $N_{\circ}.2014\text{-}1365$  dated 14 november 2014,

<sup>&</sup>lt;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)

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 result of the evaluation by the experts committee, the composition of which is specified below.

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

Unit name: Nutrition and the Brain

Unit acronym:

Label requested: UMR\_S

Present no.: UMR\_855

Name of Director

Mr Gilles MITHIEUX

(2014-2015):

Name of Project Leader

(2016-2020):

Mr Gilles MITHIEUX

# Expert committee members

Chair: Mr Louis Hue, Université Catholique de Louvain, Brussel, Belgium

Mr Pierre Fafournoux, INRA, Clermont-Ferrand (representative of the Experts:

CSS INSERM)

Mr Matthias Тschöp, Institute for Diabetes and Obesity, München,

Germany

Scientific delegate representing the HCERES:

Mr Jean GIRARD

Representatives of the unit's supervising institutions and bodies:

Ms Bénédicte Durand (representative of the Doctoral School N° 340 BMIC)

Mr Denis Fouque, Université Lyon 1

Ms Anne Rochat, Inserm

## 1 • Introduction

## History and geographical location of the unit

The present evaluation and the project follow the creation of the Inserm unit 855 and its previous evaluation in 2010. The unit is part of the Lyon 1 University, located in the Faculty Laennec.

### Management team

M. Gilles MITHIEUX (DR1) is the director of the unit.

#### **HCERES** nomenclature

SVE1-LS4

#### Unit workforce

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
N1: Permanent professors and similar positions	1	2
N2: Permanent researchers from Institutions and similar positions	3	3
N3: Other permanent staff (without research duties)	5	5
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers (Emeritus Research Director, Postdoctoral students, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)	9	4
TOTAL N1 to N6	19	16

Unit workforce	Number as at 30/06/2014	Number as at 01/01/2016
Doctoral students	6	
Theses defended	9	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	4	4

### 2 • Overall assessment of the unit

#### Global assessment of the unit

The document provided by the director of the unit reflects the exceptional quality of the research performed during the last five years. The work carried out so far extended and made the most of the previous remarkable findings of the group. In view of the relatively small size of the team, the publication record is outstanding with papers published in top journals of the field. A new paradigm is reported that changes our perception of the system controlling glucose and energy homeostasis. It offers excellent future prospects.

Briefly, the creation of murine models of tissue-specific deletion of the catalytic unit of G6Pase is a significant breakthrough that has paved the way for a better understanding of the pathology of Type 1 glycogenosis. Their previous discovery of intestinal gluconeogenesis led to the study of the possible role of this intestinal gluconeogenesis in the beneficial effects of glucose, protein-enriched diet, dietary soluble fibres and gastric by-pass on food intake, insulin sensitivity and energy homeostasis, which are mediated by gut-brain neural circuits. These original and important discoveries shed a new light on the mechanisms involved in the control of satiety and energy expenditure, and are related to the pathogenesis of Type 2 diabetes mellitus (T2DM).

#### Strengths and opportunities in relation to the context

The members of the experts committee unanimously concluded that the scientific achievements of the unit are excellent and seminal. The discoveries of the research unit changed our understanding of glucose and energy homeostasis and opened a new field of investigation in the control of the central nervous system activity by nutrients. The novelty as well as the promising future prospects of the research contributed to establish the worldwide leadership and expertise of the director of the unit.

The group has also established a fruitful collaboration with colleagues specialized in the study of gut-brain neural circuits and of the hypothalamus, which augurs well for what is to follow. This may help to consolidate the new paradigm, namely that the intestinal gluconeogenesis controls glucose and energy homeostasis, and to expend it to other control mechanisms.

The quality and the originality of the current research may also lead to a better recruitment of post-docs from abroad and to new financial support.

#### Weaknesses and threats related to the context

There are no fundamental weaknesses. A few points should be considered to consolidate the new concept.

- the importance and the physiological relevance of Intestinal Gluconeogenesis are somewhat over-interpreted and would benefit from a more precise qualification;
- the project is rather vague and lacks focus, with no clearly defined hypotheses or objectives to consolidate the new paradigm;
  - there is no exploitable medical or dietary translation of the new concept.

#### Recommendations

The new concept has not yet come of age and its credibility would benefit from a comprehensive review detailing the pros and cons.

Given the relative modest size of the unit, the number of projects should be limited and a post-doc with an established experience in neurosciences and hypothalamic studies should be recruited.

Nutritional recommendations should be considered.