



Biochimie - Nutrition humaine

Rapport Hcéres

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agence d'évaluation de la recherche
et de l'enseignement supérieur

Research Units Department

AERES report on unit:

Laboratoire de Biochimie-Nutrition Humaine
INRA USC 2012

Under the supervision of the following
institutions and research bodies:

Agrocampus Ouest



November 2011



agence d'évaluation de la recherche
et de l'enseignement supérieur

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INRA USC 2012

Under the supervision of the following
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Agrocampus Ouest

Le Président de l'AERES

Didier Houssin

Section des unités
de recherche

Le Directeur

Pierre Glorieux

November 2011

| Unit

Name of unit: Laboratoire de Biochimie-Nutrition Humaine

Acronym of unit:

Label requested:

Present no.:

Name of Director
(2008-2011): Mr Philippe LEGRAND

Name of project leader
(2012-2016): Mr Philippe LEGRAND

| Members of the committee of experts

Chair: Mr Michel LAGARDE

Experts: Mr Philippe BOUGNOUX

Ms Dominique HERMIER

Mr Michel NARCE

| Representatives present during the visit

Scientific Delegate representing AERES:

Mr Jean GIRARD

Representative of the unit's supervising institutions and bodies:

Mr Pierre-Guy MARNET, Agrocampus, Rennes

Report

1 • Introduction

Date and conduct of visit:

The visit of the unit (one team) has been operated on November 15th, 2011.

History and geographical location of the unit, and overall description of its field and activities:

The unit is a laboratory located on the Agrocampus Ouest in Rennes. The unit depends on the National School of Agronomy with a contract with INRA. Although small, the unit is well known in the field of lipid nutrition, especially for the study of long-chain polyunsaturated fatty acids deriving from the essential fatty acids in mammals, namely linoleic and linolenic acids. One important topic of research in the team is the regulation of such a metabolism by saturated fatty acids.

Management team:

The head of the team is Philippe LEGRAND, Professor of Biochemistry at the Agrocampus.

Unit workforce:

Workforce	2008-2011 Number	2012-2016 Number	2012-2016 Number of producers**
N1: Professors or assistant professors	3	4	4
N2: EPST or EPIC researchers			
N3: Other professors and researchers			
N4: Engineers, technicians and administrative staff on a permanent position	5	5	
N5: Engineers, technicians and administrative staff on a non-permanent position			
N6: Postdoctoral students having spent at least 12 months in the unit			
N7: Doctoral students	2		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended			
N10: People habilitated to direct research or similar	3	3	
TOTAL N1 to N7	10	9	4

2 • Assessment of the unit

Overall opinion on the unit:

The unit is a small size team dedicated to the metabolism and function of fatty acids of nutritional interest. This team, located at AgroCampus in Rennes, is an efficient and creative one, interacting with Rennes University and clinical facilities in Lorient. Discussions for future interactions with the human nutrition research center (CRNH) in Nantes are also ongoing.

Strengths and opportunities:

The team benefits from international recognition in polyunsaturated fatty acid biogenesis from essential fatty acids in mammals, especially in the field of desaturases. Another well identified expertise is relating to myristoylation and the desaturation process in fatty acid and sphingolipid biogenesis. The research activities are well supported by industry.

Also, the team is strongly involved in training of students of the AgroCampus as well as of the Master degree and PhD level. The technician/researcher ratio of the team is relatively high, allowing good analytical possibilities.

Weaknesses and risks:

The team is small, although a new associate professor will be recruited soon, and does not interact much with the immediate surrounding for research. The impact factor of the journals for publishing the results is relatively low if we consider the quality of these results.

Recommendations:

The team should target higher impact factor journals, expand international collaborations, and apply for national and international grants.

The number of topics investigated should be better adapted to the size of the team, with a “go/no go” management of these topics. Investigations in humans rather than rodents should be a goal as much as possible, with collaboration to be developed with CRNH in Nantes.

3 • Detailed assessments

Assessment of scientific quality and production:

The first topic deals with the “metabolism and physiological role of saturated fatty acids”. The topic is important because of the pathophysiological relevance of saturated fatty acids. The team is focusing on myristic acid that is involved in the myristoylation of some intracellular proteins (with Gly as N-terminus), which results in activation of some metabolic pathways. The team investigates the myristoylation process in desaturases involved in polyunsaturated fatty acid and sphingolipid biosynthesis. Also, critical processes such as cell signalling or apoptosis are concerned. The results obtained by the team represent a significant contribution to the current knowledge, and therefore the research carried out is highly relevant and original. Very few research laboratories have expertise in this field, especially in France.

A second topic deals with a desaturase-related enzyme, named FADS3, with unknown function. The approaches are well designed and described, with relevant experiments for the biochemistry and regulation of the enzyme. Although new aspects of FADS 3 have been found, they did not result in major outcomes and publications. The biological relevance of the FADS3 protein is investigated in the extracellular matrix where it has been located, but this appears as a source of diversion for such a small team (indeed, only one Associate Professor is in charge of this topic). This is a burning issue with an elevated risk as a highly competitive team in USA is making advances in this field.

A third topic, investigated in the past years, relates to a large collaborative programme aiming to determine, in obese volunteers, the impact of changes in the fatty acid composition of animal food products, those animals receiving linseeds in their diet. The program also involved a clinical and an INRA teams, in collaboration with the linseed agrofood industry. It took place within the scientific debate on the importance of the n-6/n-3 fatty acid ratio, and more specifically the 18:2n-6/18:3n-3 one, on the occurrence of various metabolic disorders. The nutritional approach, based on the intake of food products derived from animals fed with extruded linseed (rich in 18:3 n-3), is very relevant and original. Although this nutritional intervention resulted in a weak increase in the long-chain omega-3 derivatives, EPA & DHA, virtually no clinical effects could be observed. For these reasons and because of logistic ones relating to the collaboration with the Lorient CHR, this topic will not be further studied.

The quality of the scientific production is high, if we consider the small size of the team (all the members are producing scientists). However, at the exception of a journal with IF over 10 (Hepatology), most of the original work has been published in quite specialized journals with medium IF (Lipids, Mol Cell Biochem, Biochimie.). Several reviews (Curr Opin Clin Nutr, Biochimie, BBA Mol & Cell Biol Lipids) or expert review (Am J Clin Nutr) have also been published. Journals with higher impact factors should be targeted. The very heavy human study on the effect of fatty-acid modified animal products in obese volunteers led to only one publication, justifying that this approach be abandoned in the team project.

Assessment of the unit's integration into its environment:

The team benefits from a strong support provided by the local and national milk industry, which has been established in the Brittany Region for a long time. The team has a good national visibility, and is represented in numerous activities such as teaching and administrative responsibilities. This may explain in part the low international visibility except for the team leader.

No international grants and nor funding from national programs (ANR) could be noted. Thus, the international visibility of the team remains to be reinforced.

The team is relatively isolated in its scientific environment, and is encouraged by its institution to be more connected with local units.

Assessment of the research unit's reputation and drawing power:

The leader of the team has been invited to give a talk or a lecture in 30 meetings, including 9 international meetings or symposia, because of his expertise in saturated fatty acids and polyunsaturated fatty acid biogenesis in mammals. His expertise is also recognized as being the Vice-president of the Expert Committee of Human Nutrition at ANSES.



The recruitment of a new Associate Professor in the near future will reinforce the team and reflects its attractiveness. The relative limited international visibility of the unit may explain the absence of foreign doctoral and post-doctoral fellows, which means that attracting researchers from abroad should be encouraged. However, each scientist is involved in French PhD student training.

The team does apparently not participate in international and national programs. The financial support of the research programs is guaranteed by industrial grants. Collaboration with a Canadian laboratory is mentioned.

An effort should be made to promote the participation of young associate professors in national and international events.

Assessment of the unit's governance and life:

The size of the unit is small and therefore the organization is quite simple. Due to the small size of the team, attention must be paid to the possible isolation of young scientists (PhD students). Also, each member of the technical staff is more or less involved in all projects. However, the technicians appreciate to be, when possible, more involved in a specific project.

The scientific animation is very good, but lacks of seminars, journal clubs, invited speakers to link the activity of the team with other groups from Agrocampus. There is no doubt however that the action of the present director is efficient.

The risk taken is somehow high for all the topics studied, especially for the investigation of FADS3. A cautious management of the topics should be engaged for the survival of the team, especially for the future of the younger researchers.

The strong implication within the Agrocampus training program is the cause of a good attractiveness for Master and PhD students. However, the drawback is the heavy teaching load on the researcher/teachers and technicians.

Assessment of the strategy and 5-year project:

There is a well-defined project which derives from the first topic reported above. This project is relevant as it aims at better understanding the mechanisms underlying the effects of myristic acid on: i) the endogenous biosynthesis of long-chain polyunsaturated fatty acids from their essential precursors; ii) the biosynthesis of sphingolipids with their functional consequences on mitochondrial function and apoptosis. Due to the specific expertise of some members of the team, there is no doubt that several of the objectives can be reached. A new goal in the topic is to investigate the impact of other types of protein acylation (such as octanoylation of ghrelin), which may be less feasible in the context.

The project dealing with the second topic reported above (FADS3) is ambitious and promising but should be better structured. Reading the program, it is not clear whether the priorities are being determined. It is likely that the team will suffer from its small size. The team should then revise its strategy, and try to define priorities because the topic is highly competitive. The team should only focus on mechanistic approaches, limit dispersion as far as possible, and try to get collaborations with abroad competitors as well.

A third topic has been presented in place of that dedicated to the effect of food from linseed-supplemented animals. This new theme aims to reconsider the requirements in 18:2n-6, linoleic acid, an essential fatty acid. It takes place in the controversial debate on the respective roles of 18:3n-3 and 18:2n-6, and their ratio, in the occurrence or prevention of various metabolic disorders. This is justified by the fact that the nutritional requirements for 18:2n-6 has been assessed in the absence of 18:3n-3, and thus may have been overestimated, due to a competition for the same desaturases and elongases during their conversion into their long-chain derivatives. These investigations are planned in the rat model for studies on the fatty acid conversions and in rabbits for studying the consequences in terms of cardiovascular effects. Such a program should clearly be more promising in humans with the use of stable isotope labelled fatty acid precursors. To that purpose, a strong collaboration with the human nutrition research center (CRNH) in Nantes is advisable.

The means (use of the rat or rabbit model, and cell cultures) are present in the laboratory. Due to the small size of the team, there is an easy agreement to use these resources and no internal competition is expected for allocation of means.



The first topic (acylation of proteins) is original and may be the less risk-taking project of the team: it is well defined, carried out in a very limited number of teams in the world, and benefits from a strong expertise.

The second topic is at high risk, but may be quite fruitful if it successful.

The third one aims at revisiting the old paradigm of essential fatty acids from the viewpoint of competition between them. Its relevance would be best in being investigated in humans.

Overall, the risk associated to those different topics could be largely minimized by adopting a “go/no go” strategy, especially for the second topic, as the small size of the team might be limiting to be fully efficient at investigating the three topics.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
Biochimie - Nutrition humaine	B	A	A	A	A

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique



Statistiques de notes globales par domaines scientifiques (État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2_LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	42	5	20	26	36	59	5	17	29	239
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

* les résultats SVE2 ne sont pas définitifs au 06/05/2011.

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- SVE1 Biologie, santé
 - SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie
 - SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes
 - SVE1_LS3 Biologie cellulaire, Biologie du développement animal
 - SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie
 - SVE1_LS5 Neurosciences
 - SVE1_LS6 Immunologie, Infectiologie
 - SVE1_LS7 Recherche clinique, Santé publique
- SVE2 Ecologie, environnement
 - SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement
 - SVE2_LS9 Sciences et technologies du vivant, Biotechnologie
 - SVE2_LS3 Biologie cellulaire, Biologie du développement végétal