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GenHotel - Auvergne

Rapport Hcéres

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

Research Units Department

AERES report on the research unit

GenHotel

From the

University of Clermont-Ferrand

September 2011

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

Research Units Department

AERES report on the research unit

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From the

University of Clermont-Ferrand

Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

September 2011

Research Unit

Name of the research unit : GenHotel

Requested label : EA

N° in the case of renewal :

Name of the director : M. François CORNELIS

Members of the review committee

Committee chairwoman

Ms. Florence APPARAILLY, Université de Montpellier 1, Montpellier

Other committee members

M. Jean ROUDIER, Université d'Aix-Marseille 2, Marseille

M. Gilles CHIOCCHIA, Université Paris 5, Paris

Observers

AERES scientific advisor

M. Nicolas GLAICHENHAUS

Report

1 • Introduction

- Date and execution of the visit

The visit was organized on September 20th, 2011. It started with a general presentation by the head of the unit and was followed by several presentations by other lab members. The committee members then met with members of the research unit.

- History and geographical localization of the research unit, and brief presentation of its field and scientific activities

The project application relies on gathering clinical and biological expertises on multifactorial disorders to build a very large biobank (aiming at the follow-up of 100,000 individuals belonging to families affected by RA) for local and national projects studying the interactions between genetic and environmental risk factors. The members of the research unit do not have a dedicated lab space yet. They are clinicians and scientists from the university hospital of Clermont-Ferrand and the university of Auvergne.

- Management team

M. François CORNELIS and Ms. Isabelle CREVEAUX are the co-heads of the research unit. The unit includes a total of 4 PU-PH, 1 MCU-PH, 3 CCA, 3 PH, 1 PhD student, 1 ARC and 2 administrative assistants including 1 for the communication.

- Staff members

N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0
N3: Number of other researchers including postdoctoral fellows (Forms 2.2, 2.4 and 2.7 of the application file)	6
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	
N6: Number of Ph.D. students (Form 2.8 of the application file)	
N7: Number of staff members with a HDR or a similar grade	4

2 • Overall appreciation on the research unit

• Summary

The present project aims at conducting a follow-up in France of 100,000 individuals belonging to families affected with Rheumatoid Arthritis to (i) provide RA family members a predictive risk estimation for RA occurrence, (ii) discover novel genetic and environmental risk factors for RA, and (iii) use such cohort as prototype to study other multifactorial disorders that represent a major public health burden.

• Strengths and opportunities

• The major impact of a such project collecting sequencially biological samples from RA relatives is to provide researchers with biological materials from healthy donors that will develop RA (1/1000/year) to test any pathophysiological hypothesis.

• The medical and scientific relevance of the proposed approach is to identify (i) predictive risk factors for rheumatoid arthritis and (ii) molecular and cellular mechanisms associated with disease occurrence ;

• The ability of the two PI to build a project gathering researchers coming from different disciplines;

• The know-how of the two PI to organize the collection of biological samples ;

• The track record of one of the two PI in rheumatoid arthritis ;

• The strong links with Nutrinet, GenHotel Evry, and other international institutions ;

• The long-lasting support from the Association Française de Polyarthrite ;

• The research project focuses on two of the priorities of the university of Auvergne, i.e. genetics and nutrition ;

• The added value of this research unit for the local stakeholders including the Region Auvergne.

• Weaknesses and threats

• The success of the project will be highly dependent on a strong and long-lasting support from the local and national organizations (positions for technicians and engineers, lab space, long term sample storage, sample analysis…) ;

• Threat : the existence of other national and international cohorts focusing on rheumatoid arthritis or other inflammatory diseases.

• Recommendations

• Establish a clear-cut management policy, more specifically for ressource allocations ;

• Put some effort on the collection of samples from identical twins discordant for RA ;

• Recruit PhD students and postdoctoral fellows.

- Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	5
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	0
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	5
A4: Number of HDR granted during the past 4 years (Form 2.10 of the application file)	NR
A5: Number of PhD granted during the past 4 years (Form 2.9 of the application file)	NR

3 • Specific comments

- Appreciation on the results

The head of the lab is the coordinator of a European network that has contributed to the identification of susceptible genes for rheumatoid arthritis. The analyzed "RA relative cohort" included 10,000 individuals. In this population, the incidence is 1/1,000 per year as compared to 1 /10,000 in the overall family. In the project, the goal is to expand the cohort to 100,000 individuals (of note, there are about 4 million potential participants in France).

During the past 5 years, the members of the lab have published more than 120 papers in peer-review journals including several as first or last author. Among the most important publications in first or last author are: 1 paper in The New England Journal of Medicine (2007), 2 papers in JAMA (2009, 2010), 1 paper in PNAS (2007), 1 in Ann Rheum Dis (2008), 1 in Arthritis Rheum (2008). The scientific production is heterogeneous.

- Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners

The members of the research unit are participants to several national and international organizations.

During the past 4 years, the research unit members have been able to raise significant funds including 230 k€ from the EU, 260 k€ from various associations, 18 k€ from the industry, 315 k€ from PHRC and 118 k€ from other sources.

The research unit has developed strong links with Nutrinet and the GenHotel Evry, and the Geneva University Hospital for the recruitment of individuals. Strong links have also been developed with local, national and international structures for the analysis of the samples. These include the Centre de Ressources Biologiques, the CHU biochemistry platforms, Ultra high through put sequencing, the GenHotel Evry, the CNG-CEPH, the Karolinska Institute…

- Appreciation on the management and life of the research unit

The project of the research unit is dependent on the recruitment of 100,000 individuals. Therefore, the research unit has developed a very efficient external communication policy with several partners including local newspapers, other media, and French pharmacists and rheumatologists.

Lab meetings have been organized on a weekly basis to construct the project.

Among lab members, 5 have teaching duties and participate to the Master "Génétique et Physiology" at the University of Auvergne, the Master "Génétique" of the University Paris 7, the Master "Biologie Ostéo-articulaire" of the Universities Paris 7 and Paris 13.

- Appreciation on the scientific strategy and the project

The project is based on the recruitment of individuals who have at least one relative with rheumatoid arthritis. The objectives are (1) to document in these individuals the development of not only rheumatoid arthritis (RA), but also renal failure, anaphylaxis, birth-defect, venous thrombo-embolism (2) investigate genetic and environmental factors involved in disease onset including nutrition, smoking, infections and psychology. The specific aims are (1) to measure risk of known factors, (2) to search for new risk factors, (3) to search for biomarkers predictive of onset and (4) to identify new drug targets.

The "100,000 RA relative cohort" will be recruited mainly by the research unit in Clermont-Ferrand but also by Nutrinet-Santé, the GenHotel Evry and the Geneva CHUV. The recruitment procedure includes internet preinclusion, informed content sent by post, diagnosis confirmation by post, internet questionnaire, biological sampling and storage.

This ambitious project is highly relevant for public health and the research unit is well positioned to be successful. In the long term, this project may lead to the improved care of patients with rheumatoid arthritis, and possibly other diseases. This project could therefore have a major impact in the medical and scientific field. However, the success of the project will be highly dependent on a strong, secured, and long-lasting support for local and national organizations (positions for technicians and engineers, lab space, long term sample storage, sample analysis…).

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
GenHotel-Auvergne	A	B	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**

Reply to the AERES report on GenHotel-Auvergne, University of Clermont-Ferrand I

We thank the committee for its review and his very positive assessment.

We are grateful to the committee to have pointed out the expertise of the different members of the group and the originality of this project gathering researchers from different specialties.

We would like to add some comments regarding the report.

The representatives of the University were the vice-president Pierre-Charles ROMOND, in charge of innovation, development and entrepreneurship in the University, and Pierre CLAVELOU, vice-dean of the Medicine Faculty.

We appreciated very much the quality of the discussion with the committee and his very constructive recommendations, especially regarding the collection of samples from monozygotic twins who are discordant for rheumatoid arthritis (RA). We have added to the project a specific effort to recruit such twins. We clarify the management policy, in particular for resource allocations and aim at recruiting rapidly PhD students as well as post-doctoral fellows, as the lab space issue is about to be solved.

The committee mentioned some threats regarding the existence of other national and international collections focusing on RA. We answer that today, we are the only national research unit focusing on large scale family material for RA and unaffected relatives. Abroad, the research teams with a track record on large scale RA family material (> 1,000 families) are in Manchester and New York. Very recently, two groups started similar projects on RA relatives, in Denver and Geneva, both aiming at the much smaller scale of 2,000 relatives in the next few years. We have established a strong collaboration with the Geneva's group and together, we are the only concerted effort in Europe so far. Many other groups in France, Europe and internationally conduct cohorts focusing on RA (with no focus on their relatives). It is clear that we need to develop rapidly our resource to keep the benefice of our early start,

in the likely case of some of those strong groups deciding to add a focus on un-affected RA relatives. The stronger we will be, the more we will build on the successful collaborations with many of those groups, to have them as partners with access to our biological material, rather than competitors.

The committee noticed that the major difficulties we will have to face are the lack of technicians and engineers, the absence of dedicated lab space and long-term sample storage. We would like to mention that, despite these difficulties, we have started to work on this project with local goodwill, allowing us to get storage for 20 000 samples for DNA, serum and cells and to wait for equipment grants (local, national or international). Since the committee's visit, the rapid development of the local CRB (Centre de Ressources Biologiques) at the University Hospital has been confirmed, with sufficient space to accommodate the storage for the project and dedicated human resources (cf letter of the CRB coordinator, Pr Berger, enclosed). As far as lab space is concerned, our Dean will provide us with 50 m^2 to start. At his request, we submitted a plan aiming at the lab space indicated in our project of 300 m^2 by 2013. For strengthening the human resources, the negotiation for the critical position of assistant-professor "MCU" included in our project is under way with our Dean and our President, potential candidates being invited to apply.

We will pursue to actively request further help from the University and the CHU of Clermont-Ferrand, regarding the high relevance of our project for public health and its high potential impact in medical and scientific field, points highlighted by the committee.

21/10/2011

Isabelle Creveaux François Cornélis