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

Research Units Department

AERES report on unit:

Gene-Environment Interactions in Cardio-Vascular Physiopathology

IGE-PCV

Under the supervision of the following institutions and research bodies:

University of Lorraine

January 2012

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

Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head

Pierre Glaudes

Unit

Name of unit:	Gene-Environment Interactions in Cardio-Vascular Physiopathology
Acronym of unit:	IGE-PCV
Label requested:	UMR_S
Present no.:	EA 4373
Name of Director (2009-2012):	Ms Sophie VISVIKIS-SIEST
Name of project leader (2013-2017):	Ms Sophie VISVIKIS-SIEST

Members of the committee of experts

Chair:	Mr Jörg HAGER, Evry
Experts:	Mr Panos DELOUKAS, Hinxton, United Kingdom
	Ms Emmanuelle GENIN, Paris
	Mr Mario PLEBANI, Padova, Italy

Representatives present during the visit

Scientific Delegate representing AERES:

Mr Paul HOFMAN

Representative(s) of the unit's supervising institutions and bodies:

Ms Marie-Josèphe LEROY-ZAMIA, INSERM

Mr Pierre MUTZENHARDT, University of Lorraine

Report

1 • Introduction

Date and conduct of visit:

11th January 2012

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

The research unit (EA) 4373 'Cardio-Vascular Genetics' affiliated to Henri Poincaré University (UHP) was established on 1stJanuary 2009. The formation of this EA was the result of many years of work on the genetic epidemiology of cardio-vascular diseases, initially within Team 4 of INSERM unit 525 directed by Sophie VISVIKIS-SIEST. From this point, the aim of bringing together researchers from various disciplines (genetic epidemiology, molecular biology, immunology, pharmacology/pharmacogenomics, biostatistics/bioinformatics, setting up and managing biobanks) was to study the gene-environment interactions involved in cardio-vascular physiopathology with a family cohort as the main tool, the STANISLAS cohort (STANISLAS Family Study, SFS) set up by the team in 1993 and monitored for 15 years with the help of the Vandoeuvre-lès-Nancy Preventive Medicine Centre (CMP). This team became attached to Nancy CIC 9501, a transition period through which it was afterwards able to obtain its autonomy by forming an independent research unit. The particularity of the team is its multidisciplinary approach strategy combining genetics, transcriptomics and intermediate phenotypes. This 'translational' approach extends from determining the genetic components of intermediate phenotypes of cardio-vascular diseases and characterising the genetic variants involved to determining their interactions with environmental factors or with other genetic variants (epistasis) and finally determining their functionality. More recently, structural changes have been made in parallel with methodological transitions. Thus, in 2007, it began an approach using the new high-throughput genotyping methods which were being developed at the time. With the backing of INSERM the team wishes therefore to continue its work in the direction that has already taken by requesting the creation of a mixed INSERM/University Research Unit (UMR_S).

Management team:

Ms Sophie VISVIKIS-SIEST

Unit workforce: 20,5

Workforce	**Number** on 06/30/2011 *	**Number** on 01/01/2013 *	2013-2017 **Number of producers****
N1: Professors or assistant professors	3	3	2(+ 1 new recruitment)
N2: EPST or EPIC researchers	3	2	2
N3: Other professors and researchers	4	5	5
N4: Engineers,technicians and administrative staff*on a permanent position	4(3,5)	3(2,7)	
N5: Engineers,techniciansand administrative staff*on a non-permanent position	0		
N6: Postdoctoral studentshaving spent at least 12 months in the unit	0		
N7: Doctoral students	3		
N8: PhDdefended	4		
N9: Number of Habilitations to Direct Research (HDR)defended	6		
N10: People habilitated to direct research or similar			
TOTAL N1 to N7	**17**	**13**	**9**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the[01/01/2007-06/30/2011] period who will be present in 2013-2017.
Definitionand downloading ofcriteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

2 • Assessment of the unit

Overall opinion on the unit:

There is a good team spirit with solid scientific output. The unit has potential to further increase output by capitalising on their well phenotyped sample collections, current and future. Use of family design is a positive point making the unit more competitive at the international level ; therefore this could be extended beyond the Stanislas cohort. Use of unrelated subjects is an alternative as long as it complements current efforts by focusing on cohorts of non North European descent.

Strengths and opportunities:

• Quality of publications is increasing – the unit has established a good collaborative network and continuity on the same research line has led to improved quality of scientific output

• Good analytical capabilities within the unit and links to LORIA

• The quality of postdocs attracted by the unit is a clear strength

Weaknesses and risks:

• Expanding research activities for a relatively small unit over too many phenotypes e.g T2D is a potential risk

• Within the region and the campus the unit appeared to be somewhat isolated scientifically, may now take advantage from some recent changes, namely the merger of the Nancy and Metz Universities.

Recommendations:

• Keep the number of investigated phenotypes to a minimum to increase competitivness. Focus more on the endophenotypes of the available cohorts.

• Stanislas cohort: full set of biological specimens to be stored in two locations for security. Also, it is very important the full phenotypic information to be made available to all responsible investigators to maximise scientific output

• One declared goal of the unit is work in pharmacogenetics. The unit should seek local collaborations with clinicians in the cardiovascular field to explore the possibilities to obtain relevant samples.

• More links with university to attract masters and PhD students.

3 • Detailed assessments

Assessment of scientific quality and production:

Through the study of specific endophenotypes in well phenotyped family-based cohorts the unit has been able to generate novel insights relevant to cardiovascular risk. Their data contribution to large international efforts such as MAGIC has promoted new findings.

As outlined above research quality generated by the unit is well reflected in the quantity and quality of publications authored by the unit (the mean IF increased from 2.9 to 9.1 within 3 years) – in three publications with an IF > 5 they have a first or last author.

The unit has been active in promoting scientific communication through the running of an international conference (Santorini Conference on Prospective Biology) and a European Society of Pharmacogenetics and Theranostics. In addition, members of the unit are serving on editorial boards of journals (Drug Metabolism and drug interactions) and societies (European Society of Predictive Medicine, of which the PI is vice president).

Assessment of the unit's integration into its environment:

The unit pursues research projects with the industry (Randox), paving the way for more translational work (Biointelligence).

It promotes cultural relations with countries from the Middle East and Africa through collaborative research efforts and training of PhD students and Postdocs.

The integration with other university units working in related fields can be improved leading to more critical mass. The university has plans to provide the necessary space by 2015 to facilitate this process.

The unit has been successful in raising money through both national and EU programmes (Biointelligence). Indeed most of the unit's funding stems from external sources.

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

The unit leader has a good track record as invited speaker to national and international events (34 invitations between 2007 and 2010). The unit is lacking in a good second tier of more senior researchers with most scientists currently being junior (post-docs and PhD students).

The unit is very international with many members specifically joining the unit from abroad. This is especially true on the PhD level, where 5/6 come from abroad.

• Internationally the unit is very well connected to other groups including large international consortia on cardiometabolic traits. Some provide additional biological samples for the molecular studies of the unit.

• The international and national collaborations provide the unit also with access to some of the high-end technologies that are mostly only avaialble to large research structures and centers like genome-wide genotyping and next generation sequencing.

Assessment of the unit's governance and life:

The unit appeared to have an excellent working ambience with all members highly motivated.

The unit has initiated a number of activities through the running of an international conference (Santorini Conference on Prospective Biology) and a European Society of Pharmacogenetics and Theranostics. In addition, members of the unit are serving on editorial boards of journals (Drug Metabolism and drug interactions) and societies (European Society of Predictive Medicine, of which the Unit leader is vice president).

Assessment of the strategy and 5-year project:

The unit has access to human biological resources with good quality phenotype data that have strong potential to drive their future projects. The unit is also quite successful in obtaining funding through grant applications both on a national and international level but it will be essential to obtain core funding to ensure continuity.

A major determinant for success will be the unit's ability to keep up current collaborations with larger research centers to maintain access to the much needed high end technologies (next generation sequencing, high throughput genotyping).

The originality of the research plans lies in the focus on specific endophenotypes that the unit has priviledged access to, especially through the Stanislas cohort. The study of these endophenotypes is a logical next step in understanding the results from large scale genetic studies in cardiovascular diseases.

Assessmentof the unit's involvement in training:

- The unit is very well established within the teaching activities of the university. Many of the senior level researchers give undergraduate courses at the university.
- The PhD students are well integrated in the unit.
- To date all doctoral students, except one (activities to obtain funding are ongoing) are funded through grants or fellowships that cover the total period of their training.
- In the seperate discussions with the PhD students the panel was able to determine that all of the PhD students had very clear ideas about their immediate future after finalizing their training. Most of the foreign PhD student already had secured positions in their countries of origin or were anticipating to obtain one. The two french PhD students anticipated staying on in the unit after their training. Of note for the panel was the absence of explicit expression of interest to pursue a post-doctoral training in a foreign lab (other than returning to the country of origin) by any of the students.

4 • Grading

Once the visits for the 2011-2012 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the four criteria defined by the AERES and was given along with an overall assessment.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the overall assessment and the following grades:

Overall assessment of the unit "Gene-Environment Interactions in Cardio-Vascular Physiopathology" (IGEPCV) :

Unité dont la production, le rayonnement, l'organisation, l'animation et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	A	A	A

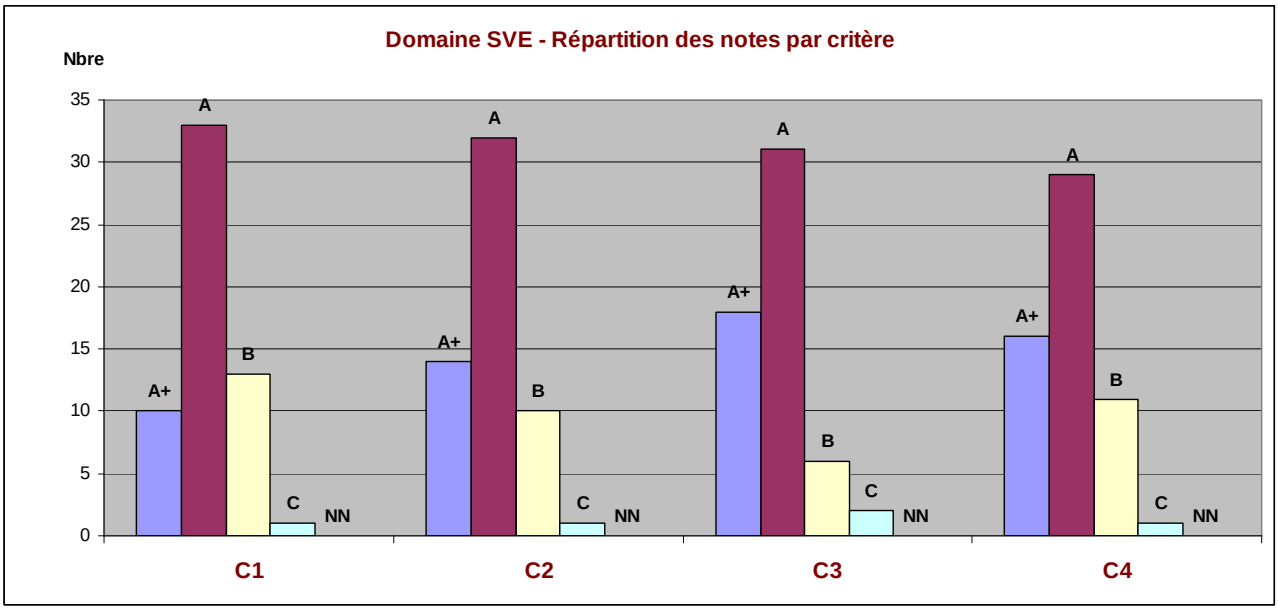
5 • Statistics per field

Notes

Critères	C1	C2	C3	C4
	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Gouvernance et vie du laboratoire	Stratégie et projet scientifique
A+	10	14	18	16
A	33	32	31	29
B	13	10	6	11
C	1	1	2	1
Non noté	-	-	-	-

Pourcentages

Critères	C1	C2	C3	C4
	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Gouvernance et vie du laboratoire	Stratégie et projet scientifique
A+	18%	25%	32%	28%
A	58%	56%	54%	51%
B	23%	18%	11%	19%
C	2%	2%	4%	2%
Non noté	-	-	-	-



6 • Supervising bodies' general comments

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Date 30/03/2012

L'Administrateur Provisoire
Jean-Pierre Finance

à

Monsieur Pierre GLAUDES
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

Objet : rapport d'évaluation de l'EA IGEPCV
Référence du document : C2013-EV-0542493S-S2PUR130004754-RT

Monsieur le Directeur,

Vous m'avez transmis le 8 mars dernier le rapport d'évaluation de l'Equipe d'Accueil « Interactions Gène-Environnement en Physiopathologie Cardio-Vasculaire (IGE-PCV) » et je vous en remercie.

Je vous prie de trouver ci-dessous les éléments de réponse de Madame S. Visvikis-Siest, directrice de l'unité.

En tant que tutelle du laboratoire nous n'avons pas de remarque particulière à émettre sur le rapport du Comité d'évaluation. Nous prenons bonne note de ses recommandations qui nous semblent tout à fait recevables à ce jour.

Je vous prie d'agréer, cher collègue, l'expression de mes sentiments distingués.

L'Administrateur Provisoire

Jean-Pierre Finance

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VOLET GENERAL

Reference: AERES report on the request for creation of a mixed INSERM/University Research Unit (UMR_S): **Gene-Environment Interactions in Cardio-Vascular Physiopathology - IGE-PCV**.

The EA-4373 has successfully received and further read the AERES report.

OBSERVATIONS of the Unit's Director:

On behalf of my team, I would like to address warm thanks to the Members of the AERES Committee of experts: their professionalism and affability allowed fruitful and convivial exchanges with our scientists.

We are pleased by their report that we consider very positive and helpful for adjusting our strategies in the future. We specially appreciated the fact that our "good team spirit" and "solid scientific output" have been acknowledged. Indeed, we focused our efforts in gathering a multidisciplinary team with individuals from different cultures and backgrounds in order to set up our translational approach of which "originality" has also been highlighted in the report. This, and the fact that we continuously adapted to new innovative technologies among the years, is at the origin of our "improved quality of scientific output".

The committee expressed very few concerns that we would like to address nonetheless:

- We could seem "isolated scientifically" within the region and the campus but as noted by the experts, we engaged since many years now fruitful collaborations with the LORIA, where we have underwent a collaborative thesis, and with several units of the CHU through the PPF «*Bio-marqueurs du Vieillissement Tissulaire*» headed by

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Pr. Athanase Bénétos. We have already published two common papers and we have three others in preparation with the PPF teams. As an example of other engaged collaborations we could cite the genome-wide association study of haptoglobin that has been very recently accepted for publication (February) and published this week in PLoS ONE conducted in collaboration with the INSERM unit U954 in Nancy. We also developed an interface contract with the hospital in order to "obtain relevant samples" for our pharmacogenetic ambitions.

- We also neglected to precise in our previous reports and during the visit that the majority of our Master and PhD students were graduated from the University of Lorraine before their involvement in the team. Only 3 PhD students come directly from abroad and all our PhD students are currently funded through grants or fellowships that cover the total period of their training.
- We would like also to clarify that an assistant professorship position is currently available in the Faculty of pharmacy of Lorraine University, hopefully for one of our post-doc students who already underwent a post-doc or graduate work outside our Unit. We are planning for another student a 2 years post-doc in close collaboration between Dr. Georg Ehret's laboratory in Geneva (leader in the genetics of blood pressure field) and our team with the aim to request a research position in INSERM. Furthermore, we think that the creation of the INSERM/University Unit would be an excellent opportunity to recruit other senior researchers consequently answering to the experts comment: "Unit is lacking in a good second tier of more senior researchers".

In the future, we plan to pursue our involvement in international consortia on cardiometabolic traits and we hope that the support of both Institutions, University and INSERM, will "ensure" this continuity through "core funding" and consolidation also of our Biological Resource Center because, as noted by the committee, "it is very important the full phenotypic information to be made available to all responsible investigators to maximize scientific output".

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Once again, given the international reputation and expertise of our Committee members, we feel honored by this report and hope that this visit, thanks to the proposed recommendations and to the Institutions support, will be a tremendous help to improve the functioning of the Unit and the beginning of a new successful chapter for our team.

Sincerely,

Dr. Sophie VISVIKIS-SIEST
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