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Equipe génomique, Bioinformatique et pathologies du système immunitaire

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit
Génomique, bioinformatique et applications
From the
Conservatoire National des Arts et Métiers (CNAM)

Mai 2010



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AERES report on the research unit
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From the
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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

Mai 2010



Research Unit

Name of the research unit: Génomique, Bioinformatique et Applications

Requested label: Equipe d'accueil

Name of the director: Mr. Jean-François ZAGURY

Members of the review committee

Committee chairman

Mr Dominique EMILIE, Université Paris 11

Other committee members

Mr Laurent ABEL, Université Paris 5

Mr Bruno CANARD, Université d'Aix-Marseille 2

Observers

AERES scientific advisor

Ms Claude-Agnès REYNAUD

University, School and Research Organization representatives

Mr Ali SAIB, CNAM



Report

1 • Introduction

The visit of the candidate laboratory took place on april 9, 2010, and lasted from 2.00 pm to 5.45 pm. It started with a general presentation by the head of the laboratory of previous researches of the group, the main achievements, the context and environment of previous works and of the present application. The scientific project was then detailed by the head of the laboratory and by younger scientists and post-docs.

This group is located in the "Conservatoire National des Arts et Métiers", and has been working so far on the genetic epidemiology of HIV-infected patients, in order to identify genetic variants associated with different rates of progression of the immune deficiency. This project has been based on the conjunction of unique cohorts of HIV-infected patients, enrolling rapidly- or slowly-progressing patients, genotyping of SNPs, and development of original bio-informatic tools. More recently, a Drug Design project has emerged, aiming at identifying candidate inhibitors of cytokines and other immunological molecules, and relying on the in silico screening of potential antagonists.

The team associates, in addition to its leader, two scientists, an administrative staff and an engineer with a permanent position, one engineer and one post-doc supported by research contract, 3 PhD and one master student. The committee was favorably impressed by the youth and enthusiasm of the team.

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.8 of the application file)	3	3



2 • Overall appreciation on the research unit

- Summary

This group has developed an original approach in the field of genetic epidemiology of HIV infection, by the conjunction of an interesting cohort of patients with a well defined follow-up, accurate analysis of genetic polymorphisms, and development of dedicated bio-informatic tools, especially for the characterization of haplotypes. Such a wide "savoir faire" concentrated in this relatively small team has allowed efficient evaluation of genetic predispositions influencing the rate of progression of immune deficiency in HIV-infected patients. The originality of the findings has been acknowledged by several publications in good specialty journal, and by the recent integration of the team in an international network dedicated to HIV genetic epidemiology. Among several expertises of the team, that in bio-informatics is probably the main strength in the international competition. The local environment (CNAM) appears especially appropriate to even improve this knowledge in bio-informatics.

Taking advantage of this expertise in bio-informatics and of the identification by genetic screening of candidate molecules of the immune system influencing the rate of progression of immune deficiency, the team has recently developed a project of drug design aiming at identifying antagonists of these candidate molecules. This approach goes directly from genetic epidemiology to attempts of drug design, without further investigations, either ex vivo or in vivo, of the functional properties of the candidate molecules. Drug design is mostly limited to in silico screening of molecules, with few if any downstream evaluations. This deliberate choice is supported by the willing of rapid valorization of hypotheses and potential drugs, an objective strongly supported by the CNAM.

- Strengths and opportunities

An active involvement in education and teaching.

An interesting combination of "savoir faire" in genetic epidemiology and development of original bio-informatic tools

The youth, competence, and enthusiasm of the team, including its leader

A strong support of the environment (CNAM), reflected by the creation of several permanent positions, and explained by the quality of the project and by its appropriateness with CNAM objectives (teaching, bio-informatics, drug development, valorization)

A good scientific production in specialty journals

- Weaknesses and threats

This team presents an ambitious program, going from genetic epidemiology to drug development, targeting several molecules of the immune system. However, this team is relatively small and appears rather isolated. This is a potential weakness for the complete validation of working hypotheses and of the properties of candidate drugs.

The willing to rapidly progress from identification of candidate targets by genetic epidemiology to drug design and valorization, without in-depth biological analysis of findings and mechanisms, may negatively impact the quality of publications. This, and the limited investigations downstream of in silico drug design, may affect the strength of potential patents.

- Recommendations to the head of the research unit

Better define priorities among target molecules of the immune system for the development of new drugs ;

Establish appropriate collaborations in two fields:

for the biological evaluation of candidate molecules of the immune system and of their function in the pathophysiology of the considered disease. Certainly, the limited size of the team and its limited expertise in experimental biology justifies that it does not engage on its own ambitious functional validation studies. However,



this could be done in association with appropriate partners, strengthening the findings of the team and the revendications of patents.

for the drug design. It is highly recommended that the team engages partnerships with laboratory experienced in drug development, immediately downstream of the in silico drug design performed by the team.

- Production results

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	3
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	NA
A3: Ratio of members who are active in research among permanent researchers $[(A1)/(N1 + N2)]$	3/3
A4: Number of HDR granted during the past 4 years	0
A5: Number of PhD granted during the past 4 years	3

3 • Specific comments on the research unit

Findings have been original, leading to several good publications in specialty journals. This originality has been acknowledged by the integration of the team in international networks of genetic epidemiology of HIV-infection.

The team has been successful in attracting young French scientists and providing some of them with permanent positions. The position of the team at the interface between epidemiology, genetics and drug design, with a strong expertise in bio-informatics, appears especially attractive. The team has been efficient in raising funds, and the local support of the CNAM is strong and promising for the strengthening of the team and its integration in the overall dynamics of CNAM laboratories.

The team has a strong teaching activity. All members of the team share the project with enthusiasm and efficacy, as well as competence, in a strategic field, bio-informatics. Students are well integrated, and appropriately supported.

The project is interesting and original, and feasible considering the expertise and enthusiasm of team members. It has to be implemented by establishments of new collaborations in experimental biology and in drug development.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	A	A

Paris, le 4 juin 2010

Le Directeur de la Recherche

à

Monsieur Pierre Glorieux
Directeur de la section des unités de
recherche
Agence d'Evaluation de la Recherche et de
l'Enseignement Supérieur
20 rue Vivienne
75002 PARIS

Réf: DR/2010-075

Monsieur le Directeur,

Je vous remercie pour l'envoi du rapport du comité de visite concernant l'unité de recherche « Equipe génomique, bioinformatique et pathologies du système immunitaire ».

Vous trouverez ci-joint un document relatant les observations faites à ce sujet.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de toute ma considération.



Ali Saïb
Directeur de la Recherche
Cnam
292 rue Saint-Martin
75141 PARIS CEDEX 03

Veillez trouver ci-dessous les éléments de réponse concernant le rapport sur l'unité « Equipe génomique, bioinformatique et pathologies du système immunitaire » Directeur Jean-François Zagury :

Réponse suite au rapport fait par l'AERES.

Erreurs factuelles : Néant

Observations générales :

Le rapport est très bien fait et nous paraît très juste.

Notre équipe vient de se constituer et c'est seulement maintenant que nous produisons beaucoup d'information grâce aux outils bioinformatiques que nous avons mis sur pied. Nous avons établi une base expérimentale a minima pour tester nos hypothèses de travail (notamment l'évaluation des produits criblés in silico) et nous comptons effectivement lancer des collaborations avec d'autres équipes expérimentales pour exploiter de manière plus poussée les résultats obtenus.

Answer following the AERES report.

Factual errors : none

General observations :

The report is well done and seems very accurate to us.

Our team has just been built up and it is only now that we produce lots of data thank's to the bioinformatics tools that we have set up. We have also set-up an experimental lab a minima to test our working hypotheses (such as the evaluation of hits identified in silico) and we indeed consider to start collaborations with other experimental teams to exploit more deeply the results obtained.