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IAB - Centre de recherche oncologie , développement - institut Albert Bonniot de Grenoble

Rapport Hcéres

► **To cite this version:**

Rapport d'évaluation d'une entité de recherche. IAB - Centre de recherche oncologie , développement - institut Albert Bonniot de Grenoble. 2015, Université Joseph Fourier - Grenoble - UJF, Institut national de la santé et de la recherche médicale - INSERM, Centre national de la recherche scientifique - CNRS. hceres-02033940

HAL Id: hceres-02033940

<https://hal-hceres.archives-ouvertes.fr/hceres-02033940>

Submitted on 20 Feb 2019

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HCERES

High Council for the Evaluation of Research
and Higher Education

Research units

HCERES report on research unit:

Institute Albert Bonniot

IAB

Under the supervision of
the following institutions
and research bodies:

Université Joseph Fourier - Grenoble - UJF

Institut National de la Santé et de la Recherche

Médicale - INSERM

HCERES

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

Marc PARMENTIER, chairman of the committee

Under the decree N.2014-1365 dated 14 november 2014.

¹ The president of HCERES "countersigns the evaluation reports set up by the experts committees and signed by their chairman." (Article 8, paragraph 5)

² 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: | Institute Albert Bonniot |
| Unit acronym: | IAB |
| Label requested: | UMR_S, UMR |
| Present no.: | UMR_S823 |
| Name of Director (2014-2015): | Mr Christian BRAMBILLA (up to 30 September 2014) Mr Pierre HAINAUT (from 1st October 2014) |
| Name of Project Leader (2016-2020): | Mr Pierre HAINAUT |

Expert committee members

| | |
|----------|---|
| Chair: | Mr Marc PARMENTIER, University of Brussels, Belgium |
| Experts: | Mr Claude BEAUDOIN, University of Clermont-Ferrand (representative of the INSERM) |
| | Mr Hinrich GRONEMEYER, Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch (representative of the CoNRS) |
| | Ms Mirna PEREZ-MORENO, Spanish National Cancer Research Center Madrid, Spain |
| | Mr Christoph PLASS, German Cancer Research Center (DKFZ), Heidelberg, Germany |
| | Mr Andrew POVEY, University of Manchester, UK |
| | Mr Frank SEEBER, Robert Koch-Institut, Berlin, Germany |
| | Ms Joëlle SOBCZAK-THEPOT, Université Pierre & Marie Curie, Paris (representative of the CNU) |
| | Ms Corinne TANCHOT, Université Paris Descartes |

Scientific delegate representing the HCERES:

Mr Jean ROSENBAUM

Representatives of the unit's supervising institutions and bodies:

Mr Alain BUISSON (representative of the Doctoral School CSV - ED n°218)

Mr Alain EYCHENE, CNRS

Mr Yassine LAKHNECH, Université Joseph Fourier

Ms Marie-Josèphe LEROY-ZAMIA, Inserm

1 • Introduction

History and geographical location of the unit

The Institute Albert Bonniot was created in 2007 with a main research focus dedicated to similarities and shared mechanisms between normal development and cancer (“Ontogenesis and Oncogenesis”). It is located in a 4444 sq meter building on the Health Campus of Université Grenoble-Alpes, next to the Centre Hospitalo-Universitaire (CHU) of Grenoble. It is presently composed of 13 teams organised in two departments (“Différenciation et transformation cellulaire” and “Oncogénèse et biotechnologie”). The number of teams will increase to 17 according to the proposal, organised in three departments (“Signaling through chromatin”, “Microenvironnement, cell plasticity and signaling” and “Prevention and therapy of chronic diseases”). Ten of the previous teams are proposed for renewal, one with a new team leader. Five new teams will be led by scientists originating from other IAB teams or from other institutes from Grenoble. In addition, two team leaders were attracted from Nantes and Paris. As the present IAB building will not support the planned increase in team numbers, some of the new teams will be located in a nearby building of the Health Campus (Jean Roget building).

The scientific environment of IAB is excellent, comprising the Institute of Structural Biology (IBS), the Institute of Life Science Research and Technologies (IRTVS), the Grenoble Institute of Neuroscience (GIN), the Interdisciplinary Laboratory of Physics (LiPhy), the Departments of Molecular Pharmacology (DPM) and of Molecular Chemistry (DCM) of Université Grenoble-Alpes/Université Joseph Fourier (UGA/UJF) and the Laboratoire d’Electronique des Technologies de l’Information of CEA (CEA-LETI), all structures with which the IAB develops collaborations. The IAB hosts four technological platforms, including Optical Microscopy/Cell Imaging (MicroCELL), Bioinformatics (EpiMed), Imaging in live animals (OPTIMAL) and Animal Advanced Technologies (PHTA) in addition to the common animal house. It also supports two shared facilities with other nearby structures, Flow Cytometry and Molecular Detection in Situ (MDiS).

Management team

Mr Christian BRAMBILLA was director of the IAB from 2007 to September 30, 2014. Mr Pierre HAINAUT took over on October 1, 2014, and is proposed as director for the next period. The director is responsible for the scientific strategy, the administrative management, representation in official committees and external bodies and general communication. A vice-director is responsible for the coordination of infrastructure and logistics. IAB has since 2011 a Director of administration, finances, human resources and logistics who supervises a team that includes seven budget assistants, one human resource officer, four technical/logistical support staff and one assistant/secretary. The main structure assisting the director is the “Steering Committee” (replacing the former “Management Committee”). It is composed of the three directors, team leaders and Department heads, one elected representative of each staff category (researchers, professors/lecturers, ITA/ITOS and students) and *ad hoc* members designated by the director for specific missions. It meets at least 6 times a year, and discusses most aspects of the Institute’s life, including rules of procedures, scientific and social animation, platform development and management, staff development and training, allocation of resources. A new “Science and Strategy Committee”, composed of the three directors, team leaders and department heads, and meeting on a monthly basis, will assist the direction in all aspects of science and strategy, including risk-taking scientific initiatives, prioritization of applications for permanent positions and grants, allocation of shared resources and space. The “Senior Leadership Group” replaces the former “Executive Board”. It is composed of the three directors, the Department heads and three senior scientists appointed by the director, and assists the management in running the Institute. A “General Assembly” is held at least once a year. A Scientific Advisory Board (SAB) assists the direction in strategic planning. It is composed of six renowned scientists from France (2 members), Germany, Switzerland, Italy and Sweden, as well as observers from INSERM, CNRS and UGA/UJF. This SAB was consulted for defining the strategy proposed for the next period.

Overall, the expert committee felt that the Institute is very well managed and that the changes made by the new director are improving the organisation significantly. It is however difficult to appreciate entirely how the life of the Institute will change as a result of this new organisation and management, as some of the proposed measures are not yet implemented. Nevertheless, it was felt that moves are being made in the right direction.

HCERES nomenclature

SVE1_LS1 Biologie moléculaire et structurale, biochimie

SVE1_LS4 Physiologie, physiopathologie, biologie systémique médicale

SVE1_LS3 Biologie cellulaire, biologie du développement animal

SVE1_LS7 Epidémiologie, santé publique, recherche clinique, technologies biomédicales

SVE1_LS6 Immunologie, microbiologie, virologie, parasitologie

Unit workforce

| Unit workforce | Number as at 30/06/2014 | Number as at 01/01/2016 |
|--|---------------------------|-------------------------|
| N1: Permanent professors and similar positions | 32 | 36 |
| N2: Permanent researchers from Institutions and similar positions | 34 (33,3 FTE) | 40 |
| N3: Other permanent staff (without research duties) | 54 (51,4 FTE) | 61 |
| N4: Other professors (Emeritus Professor, on-contract Professor, etc.) | 7 | |
| N5: Other researchers (Emeritus Research Director, Postdoctoral students, visitors, etc.) | 12 | |
| N6: Other contractual staff (without research duties) | 48 (45,8 FTE) | |
| TOTAL N1 to N6 | 187 (181,5 FTE) | 137 |

| Unit workforce | Number as at 30/06/2014 | Number as at 01/01/2016 |
|---|-------------------------|-------------------------|
| Doctoral students | 43 | |
| Theses defended | 56 | |
| Postdoctoral students having spent at least 12 months in the unit | 8 | |
| Number of Research Supervisor Qualifications (HDR) taken | 12 | |
| Qualified research supervisors (with an HDR) or similar positions | 58 | 57 |

2 • Overall assessment of the unit

Global assessment of the unit

The IAB is composed of a set of excellent teams active in cell biology, epigenetics and translational research. The scientific output is impressive, both quantitatively and qualitatively. A new director, with very strong international reputation and management skills, was recruited recently. The new management has initiated a very effective process of reorganisation of the Unit, with the advice of a newly appointed Scientific Advisory Board. New teams and team leaders were proposed, together with a shift in the general research focus from “Development and cancer” to “Epigenetics, chronic diseases and cancer”. The ongoing changes should provide more cohesion to the Unit, as well as an enhanced capacity to establish a strong institutional scientific strategy for the future. Among the 17 teams proposed for the next period, seven are either new teams created around promising young investigators, or teams imported from other structures. A significant addition to the Unit is the recruitment of three excellent teams active in the study of parasites of the phylum Apicomplexa (*Toxoplasma* and *Plasmodium*). The Institute is located in

a very strong scientific environment and benefits from an outstanding set of technological platforms. Among the main assets of IAB are the very close links with clinicians of the nearby Grenoble Hospital and the strong involvement of its teams in clinical and epidemiological studies. The output of IAB is also exceptional in terms of patent applications, development of new diagnostic tools and therapeutic agents, and the creation of spin-off companies. Overall, the expert committee felt that the Institute will likely continue over the next 5 years to generate excellent science and increase further its attractiveness and international visibility.

Strengths and opportunities in relation to the context

The IAB is located in an **excellent scientific environment**, including the nearby Grenoble Medical Center with which important links have been established in translational research, and other renowned Institutes such as the Institute of Structural Biology (IBS) and the Laboratoire d'Electronique des Technologies de l'Information of CEA (CEA-LETI). This environment is the basis for efficient scientific collaborations and the establishment of common resources, particularly shared technological platforms.

The Institute has a **strong and clear scientific strategy**. The newly recruited director has excellent management skills and has initiated a very effective process of reorganisation of the Unit. A shift in the general research focus was proposed, from "Development and cancer" to "Epigenetics, chronic diseases and cancer" in order to adapt the translational research of the Institute to the patient recruitment profile of the nearby Centre Hospitalier Universitaire (CHU) of Grenoble. The broad scientific objective is to understand which epigenetic modifications drive the expression of (normal and) pathological phenotypes, and to develop diagnostic and therapeutic strategies based on the interplay between diseased cells, their (epi)genome and their environment.

This strategy is supported by an **international Scientific Advisory Board (SAB)** composed of high profile scientists and scientific administrators. The SAB has played an important role in the recent reorganisation of the Unit and constitutes an asset for the future, by helping the management to establish the scientific strategy of the Institute and in the recruitment of new team leaders.

New management structures were proposed, clarifying the decision-making processes, and reinforcing the role of the director. These structures are better adapted to the increased size of the Institute, and should allow the rapid implementation of new policies suggested by the SAB.

There is a strong commitment of the new management to evolve toward a **better cohesion of the Institute**, and to provide the Unit with the capacity of developing a **strong institutional scientific strategy**, such as the support of high-risk innovative projects. This will involve a redistribution of recurrent funds in favor of common structures (platforms and departments), the implementation of an overhead policy on grants, and new procedures allowing the (re)allocation of staff and surfaces.

The Institute hosts a number of **outstanding teams**, and the overall **scientific output** is impressive both quantitatively and qualitatively. Many IAB scientists have strong international visibility in their fields, including epigenetics, cell biology, environmental epidemiology and translational research, which results in a strong **attractiveness** of the Institute as a whole.

Excellent new teams are also proposed to join the Unit. These include three groups active in the study of parasites of the phylum Apicomplexa (*Toxoplasma*, *Plasmodium*). This constitutes a rare opportunity to create in this research area a very powerful critical mass that is almost unique in Europe, and favors the interaction of these teams with the strong epigenetic component of IAB.

The IAB teams have maintained a **good balance between basic science and efficient translational approaches**. Strong connections with clinicians have been established, allowing biobanking of very valuable material, and a deep involvement of the Unit in clinical trials and the development of therapeutic agents, diagnostic tools and biomarkers. The Institute has also an **exceptional output in terms of technology transfer** (patent applications, licensing, creation of start-up companies).

The Unit has also demonstrated its **high efficiency in attracting financial support**, from governmental agencies, charities and more particularly from the European Union.

The IAB has developed an **excellent set of technological platforms** with state of the art equipment. The privileged access to these platforms and the corresponding expertise constitute an invaluable asset for all IAB projects.

The IAB has a **strong and highly motivated support staff**, committed to delivering the best service to the scientists. There appears also to be a **very good Institute spirit** and a friendly atmosphere. The activity of IAB teams

is **highly collaborative**, within the Institute, but also with the Grenoble Medical Center, other research structures of the Grenoble area, and other national and international groups.

The willingness of **CNRS to become a stakeholder** for the whole Institute constitutes an interesting opportunity for IAB.

Weaknesses and threats related to the context

No major weaknesses were identified by the committee. Some of the obvious threats are linked to external factors affecting French science in general. These threats were identified by the management and were considered in the report of the unit, with proposed solutions to limit their impact.

Probably the most significant weakness is the **low number of post-doctoral fellows** in the Unit (4 % of total staff), particularly foreign fellows. This number has actually decreased since the beginning of the previous 5-year period. This situation does not reflect the excellent environment and the international recognition of IAB teams, which should allow the Unit to attract many more post-doctoral fellows from abroad. The recruitment is partly hampered by the combination of European and French regulations, which limit practically the duration of post-doctoral positions to 3 or 4 years, and by the limited number of positions funded through grants. This is however a significant issue, as post-doctoral fellows are often in the most productive period of their career, and can represent a very significant workforce and source of innovation for an Institute such as IAB. Care should therefore be taken to improve the recruitment of this category of staff in the future.

There is also a **relatively low proportion of PhD students** (19 % of total staff). The number of IAB scientists holding an HDR should allow more PhD students to be attracted. This might be increased, for example through international calls and specific partnerships with foreign institutions.

Another relative weakness is the present **lack of in-house capacity in bioinformatics and NGS technologies**. This should constitute a clear priority for additional staff linked to the EpiMed platform offering unique epigenetic datasets for bioinformatics analysis.

Despite an overall increase in the core funding, received mainly from INSERM and the UGA/UJF, the proportion of expenses allocated to staff salaries has increased progressively, reducing the funds available for the support of common structures and specific teams. The Unit and its teams will therefore **depend more deeply on external grants** in a scenario where funding faces overall reductions in France (with for example a decrease of the ANR budget). Funding the structure at an adequate level for meeting its ambitious objectives and developing a strong institutional strategy will therefore remain a permanent challenge for the IAB.

With the increase in the number of teams and the space limitation in the main building of IAB, a larger proportion of the groups will be located outside this building, **disrupting geographical unity**, and proximity to the common technological platforms. Care should be taken to maintain a common spirit among the teams located on different sites.

The excellent technical platforms constitute a major asset of IAB. It will however be a permanent challenge to **maintain these platforms competitive and up to date**, through the upgrade/maintenance of existing equipment and the acquisition of new ones.

A number of present team leaders will **reach the age of retirement** within the next 5 to 10 years. This will require their replacement by other team leaders pursuing the same scientific goals, but also the recruitment of new PIs importing their own research themes.

The present management is planning to modify significantly the way financial and staff resources are allocated to individual teams, with a reinforcement of common structures. This is a necessary move to allow the development of a strong institutional strategy. To be fully efficient, such change will however require the **full adhesion of the different teams** to this policy, and a deep endorsement of the reallocation of resources to joint ventures.

The IAB is mostly visible through the international recognition of its individual teams, but presently **lacks a strong institutional image**. This should be improved in the future.

Recommendations

The committee strongly supports the present director and managing team, as the process to reorganise the Institute and incorporate new teams with high potential has been fast and efficient. **This strategy should be pursued**,

and a number of **proposed changes should be implemented** in the near future. The important role of the international Scientific Advisory Board in this process should also be maintained in the future.

In particular, the ongoing process of reinforcing the cohesion of the Institute should be led to completion, by **investing more resources** (support staff, equipment, recurrent funds) **into existing technological platforms** and new ones as needed, and by **implementing the overhead policy** for some grant categories. One of the priorities should be the **staffing of the Epimed platform** with a bioinformatics engineer. Care should also be taken to (re)allocate support staff to groups on the basis of present scientific staff and output.

In the future, molecular diagnostics will heavily rely and include epigenetic profiling. Since the Institute will have a main pillar in epigenetic analysis and translational activities in lung cancer and other tumor entities the committee suggests the management to consider the **investment into epigenetic profiling technologies** (e.g. Illumina human 450K bead array and/or NGS) **and the needed bioinformatics platform**, in order to prepare for future developments and to place their research teams at the forefront of translational molecular epigenetics.

The creation of new independent teams led by young scientists with an excellent track record is proposed by the Institute's management. The committee supports this early recognition of talented scientists. However, the committee would recommend to establish **mentoring of these young team leaders** by more experienced scientists of the Institute working in the same field, in order to keep these teams in focus and prevent the pursuit of too diverse or overambitious goals. Future recruitment of new team leaders should preferentially be made through international calls, with the help of the SAB.

The IAB should **increase its recruitment at the international level, particularly for post-doctoral fellows**, but also for PhD students. **Increasing the proportion of post-doctoral fellows** should be another priority of the Unit. **The use of English** in the daily life of the Institute should be further reinforced to attract foreign fellows. Requests should be made to the doctoral schools for translating their regulations into English.

The IAB is known essentially through its teams, and less as an Institute. In order to make the Institute and its teams more attractive, it will be wise to establish a strategy to **increase the international visibility of the Institute as such**, through the organisation of international calls for PhD students, post-doctoral fellows or new team leaders, or the organisation of international meetings and summer schools in the name of the Institute. In the same line, the way the IAB is presenting itself to the outside world through its website should be improved.

A number of concerns raised by ITA/BIATSS staff should be addressed by the management, such as Unit policies for acknowledgements in publications, technical staff assignment changes, annual evaluations, and technician training.

The Unit is presently supervised by INSERM and the Université Joseph Fourier. Up to now, only one team had received the CNRS label. Provided the present activities of the Unit, and the recruitment of several teams labelled CNRS, and/or headed by CNRS researchers, the CNRS has expressed interest in sharing the supervision of the whole Unit, together with INSERM and the University. The expert committee fully supports this **extension of the CNRS label to the whole unit**. This is amply justified by the strong involvement of many IAB teams in fundamental cell biology, and by the large number of CNRS scientists who will join the Unit during this next period. There are also many interactions, established or planned, between the (future) CNRS and INSERM teams of the Unit.