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Immunologie des tumeurs et immunothérapie du cancer

Rapport Hcéres

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

Department for the evaluation of
research units

AERES report the research unit:

Tumor immunology and immunotherapy

Under the supervision of the following
institutions and research bodies:

Université Paris-Sud

Institut National de la Santé Et de la Recherche

Médicale - INSERM

Institut Gustave Roussy





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

Department for the evaluation of
research units

*On behalf of AERES, pursuant to the Decree
of 3 november 2006¹,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the
evaluation of research units department

On behalf of the expert committee,

- Ms Muriel MOSER, chair of the
committee

¹ The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n° 2006-1334 of 3 November 2006, as amended).



Evaluation report

This report is the result of the evaluation by the expert 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: Tumor immunology and immunotherapy

Unit acronym:

Label requested: UMR_S

Present no.: UMR_S1015

Name of Director
(2013-2014): Ms Laurence ZITVOGEL

Name of Project Leader
(2015-2019): Ms Laurence ZITVOGEL

Expert committee members

Chair: Ms Muriel MOSER, Université Libre de Bruxelles, Belgium

Experts:

Mr Vincenzo BRONTE, University of Verona, Italy

Mr François LEMOINE, Université Pierre & Marie Curie, Paris
(representative of CNU)

Mr Frédéric RIEUX-LAUCAT, Inserm (representative of Inserm)

Mr Peter VANDENABEELE, VIB, University of Gent, Belgium

Scientific delegate representing the AERES:

Mr Joost VAN MEERWIJK

Representatives of the unit's supervising institutions and bodies:

Mr Christian AUCLAIR (Doctoral School n° 418, Université Paris Sud)

Mr Etienne AUGE, Université Paris Sud

Ms Laurence PARMANTIER, Inserm

Mr Eric SOLARY, Institut Gustave Roussy



1 • Introduction

History and geographical location of the unit

The U1015 INSERM entitled “Immunology of tumors and cancer immunotherapy” was created more than 12 years ago. It focuses on designing cancer vaccines and acquired an expertise in dendritic cell and exosome biology from the bench to the bedside. It is located at the Institut Gustave Roussy and occupies 300m² at the 12th floor.

Management team

The unit is headed by Prof. Laurence ZITVOGEL, who was already re-conducted twice. It included only one team but has recently welcomed an ATIP-Avenir researcher, who was a former PhD student of the unit. U1015 will therefore be composed of two separated and independent groups for the next four years.

AERES nomenclature

SVE1_LS6 Immunology, microbiology, virology, parasitology

SVE1_LS7 Epidemiology, public health, clinical research, biomedical technologies

Unit workforce

| Unit workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|--|-------------------------|-------------------------|
| N1: Permanent professors and similar positions | 2 | 2 |
| N2: Permanent researchers from Institutions and similar positions | 1 | 1 |
| N3: Other permanent staff (without research duties) | 3 | 3 |
| N4: Other professors (Emeritus Professor, on-contract Professor, etc.) | | |
| N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.) | 4 | 7 |
| N6: Other contractual staff (without research duties) | 4 | 5 |
| TOTAL N1 to N6 | 14 | 18 |

| Unit workforce | Number as at 30/06/2013 | Number as at 01/01/2015 |
|---|-------------------------|-------------------------|
| Doctoral students | 4 | |
| Theses defended | 9 | |
| Postdoctoral students having spent at least 12 months in the unit | 5 | |
| Number of Research Supervisor Qualifications (HDR) taken | 1 | |
| Qualified research supervisors (with an HDR) or similar positions | 3 | 2 |



2 • Overall assessment of the unit

The global assessment of the unit is outstanding. The unit has proposed original concepts that will likely have an important impact in the field of cancer immunotherapy, hence on the treatment of patients suffering of various malignancies. The unit has proposed and demonstrated in mouse models a strong relationship between chemotherapy and the immune system. It has shown that chemotherapy renders tumors immunogenic under some conditions, an observation that opens new strategies for optimal combination of chemo- and immunotherapy. This concept has been suggested in humans by several reports, including those from the unit, revealing the activation of an immune response in patients after chemotherapy. Whether most “spontaneous” tumors in humans can elicit an efficient immune response and what combination of therapy should be envisaged to provoke tumor regression are important questions that deserve further investigations.

In addition, the unit has made several seminal observations that may have a direct link to the development of therapeutic approaches in the future: the characterization of IKDCs, which combine the function of DC and the killer activity of NK cells; the role of NK cells in tumor rejection; the identification of clinically relevant tumor antigens; the role of the microbiota in the success of chemotherapy; the analysis of the cellular components of the tumor microenvironment, the study of the mode of action of novel immune checkpoints blockers, etc.

The perspectives proposed by the unit are mainly the continuation of their preclinical and clinical studies, without defining a clear priority at this stage. The results of the experimental models define in a generative way the path for further research.

Strengths and opportunities related to the context

The unit has proposed several seminal concepts on the link between chemotherapy and immunity and is internationally a leading group.

The unit is involved in basic as well as clinical research.

The unit is tightly linked with a Centre of Clinical Investigation in Biotherapy (CIC-BT) in partnership with Curie Institute allowing to implement clinical trials.

The unit has established a national and international network of collaborations with internationally recognized laboratories.

The unit has received full support from the “Institut Gustave Roussy” (IGR) for the development and maintenance of the research platforms; IGR appointed a chief engineer in the unit.

The unit has obtained the funding necessary for the research in the next years and has raised institutional, private and industrial grants that represent a very substantial financial support.

Weaknesses and threats related to the context

The molecular mechanisms underlying the efficacy of the immune response triggered by chemotherapy are still elusive, whereas their identification may sustain a more targeted approach to the clinic.

The basic and clinical research relies mainly on the director of the unit.

Recommendations

The expert committee feels that the unit would benefit from the help of a molecular biologist, as a deeper understanding of molecular mechanisms would facilitate and accelerate the translation of the mouse studies to the clinic.

The expert committee recommends to two senior researchers to pass their “Habilitation à diriger des recherches” (HDR) to be able to directly supervise PhD students.



3 • Detailed assessments

Assessment of scientific quality and outputs

In the past 5 years, the unit has published several seminal publications and made several important discoveries providing insights into the effect of chemotherapy on immune tumor resistance. The research is highly original and the observations in preclinical models and in cancer patients have been published in the best international journals (Science, Nature Medicine, Cell, Nature, Cancer Research, etc.). The research of the unit has a major impact in the field, as it opens new perspectives in the treatment of cancer patients, in particular the combination of chemo- and immunotherapy, which should work in synergy.

The expert committee has been impressed by the new concepts proposed and developed by the unit and by the high number of publications in high-ranked journals.

Assessment of the unit's academic reputation and appeal

The unit is recognized internationally as expert in the field and is implicated as either coordinator or partner in several national and international consortia. In particular, the unit received two LABEL LIGUE, obtained five INCA grants as coordinator, an ANR emergence grant as coordinator, and it is part of large multidisciplinary projects (SIRIC Socrates, LABEX OncoIMMunol). The director is chairing the “Immunopôle” at IGR and created with four colleagues the European Academy of Tumor Immunology (EATI) to “promote tumor immunology at the scientific and clinical level”.

The unit has recruited an “ATIP-Avenir” researcher, who will develop as an independent investigator within the unit, and has been able to attract several (eight are presently in the unit) postdoctoral researchers, among them foreigners (from UK, Italy and Japan).

The director of the unit has launched a scientific journal “Oncoimmunology” which has published already important reports in the field, and is author of several review articles that are considered as references in the field.

Finally, the director of the unit is member of the Academy of Medicine and of the European Academy of Science in Oncology and has been granted several major prizes (from INSERM, FRM, Academy of Science).

For all these reasons the expert committee found the unit’s academic reputation outstanding.

Assessment of the unit's interaction with the social, economic and cultural environment

The unit has granted several patents and has established collaborations with four companies, and in particular a close collaboration implying a stage of a researcher in the unit for 2 years.

The unit performs experiments in collaboration with two other internationally recognized laboratories (in USA and in Australia). This long-term collaboration reinforces the impact of the concepts, as it strengthens the results in different laboratory environments and allows the use of several tumor models.

No accreditation and/or certification of procedures have been mentioned, but standard operating procedures (SOP) must have been implemented to obtain authorization from regulatory agencies in order to carry out the different clinical trials.

Overall, the unit’s interaction with the social, economic and cultural environment was excellent.



Assessment of the unit's organisation and life

The whole expert committee met the different workforces of the unit, in the absence of the director. The members of the unit were very positive about the management of the unit, which is organized to reach efficiently the scientific objectives. All members apparently feel implicated in the scientific decisions (analysis of results and proposed workplan), and are informed during frequent meetings. The pooled budget seems to be allocated according to clear scientific priorities.

The unit strongly supports (financially and scientifically) a new team created by an ATIP-AVENIR researcher.

The expert committee found the unit's organisation and life excellent

Assessment of the unit's involvement in training through research

Nine PhD students defended their thesis during the five-year contract and four theses are in progress. The minimal requirement for the thesis is "at least one paper in a peer-reviewed journal", a criterion that has been met during the last 5 years.

Seven postdoctoral researchers are presently working in the unit.

The director of the unit is teaching in Master 2 and in DESC of onco-immunology.

The chair of the Doctoral School (ED n°418) of the Université Paris Sud confirmed the high quality of the student guidance in the unit and the follow-up of the doctors after their PhD to help their integration.

During their meeting with the expert committee, the PhD students and postdoctoral researchers declared that they were involved in the internal discussions regarding the scientific progresses and the future plans; the postdoctoral researchers also participate to the grant writings.

The expert committee found the unit's involvement in training through research outstanding

Assessment of the strategy and the five-year plan

The five-year plan is an extension of the results and concepts developed by the unit during the last five years.

The strategy of the unit is to create a close collaboration between three laboratories (the unit, a laboratory in USA and a laboratory in Australia) to pursue in parallel the same scientific and clinical objectives. The director prefers at this stage not to define priorities, but to keep the same four research endpoints: the viral signature during immunogenic cell death, the design of clinically relevant tumor antigens, the link between mucosal immunity and anticancer immune responses, and the tumor interactome.

Although the project is highly consistent and of major interest, in consideration of the IGR mission, the expert committee feels that (a) priority(ies) should be defined in a near future, in order to favour a more targeted approach towards clinical applications. The impact on cancer immunotherapy may benefit from a more prioritized approach. The committee also believes that the molecular mechanisms underlying the concepts deserve further investigation.

Nevertheless the project, which keeps its originality and competitiveness, was assessed as excellent.



4 • Conduct of the visit

Visit date:

Start: Friday, January 31th 2014 at 08.00 am

End: Friday, January 31th 2014 at 05.00 pm

Visit site:

Institution: Institut Gustave Roussy

Address: 114 rue Edouard-Vaillant, Villejuif

Programme of visit:

| | |
|-------------------|---|
| 08.00 to 08.30 am | Closed-door meeting: expert committee members and AERES Scientific Delagate (DS), Mr Joost VAN MEERWIJK |
| 08.30 to 10.30 am | Presentation of past activity and projects of the unit by Ms Laurence ZITVOGEL (director) |
| 10.30 to 11.00 am | Coffee break |
| 11.00 to 11.20 am | Meeting of expert committee members and DS with engineers, technicians and administrative assistants |
| 11.20 to 11.40 am | Meeting of expert committee members and DS with PhD students |
| 11.40 to 12.00 pm | Meeting of expert committee members and DS with postdoctoral fellows |
| 12.00 to 12.15 pm | Meeting of expert committee members and DS with staff-scientists (in absence of director) |
| 12.15 to 12.45 pm | Meeting with representatives of the supporting Institutions: <ul style="list-style-type: none">- Mr Etienne AUGÉ, Université Paris Sud- Ms Laurence PARMANTIER, Regional Administrator Inserm- Ms Stéphanie POMMIER, “chargée de mission” Inserm CSS7- Mr Eric SOLARY, director research “Institut Gustave Roussy” |
| 12.45 to 01.00 pm | Meeting with the representative of the Doctoral School (ED 418) of the Université Sud Mr Christian AUCLAIR, director |
| 01.00 to 02.00 pm | Lunch-buffet |
| 02.00 to 02.30 pm | Closed-door meeting of the expert committee members and DS |
| 02.30 to 03.00 pm | Closed-door meeting of the expert committee members and DS with the unit’s director |
| 03.00 to 05.00 pm | Closed-door meeting of the expert committee members and DS |



5 • Supervising bodies' general comments

Le Président de l'Université Paris-Sud

à

Monsieur Pierre GLAUDES
Directeur de la section des unités de recherche
AERES
20, rue Vivienne
75002 Paris

Orsay, le 9 juillet 2014

N/Réf. : 156/14/JB/LM/AL

Objet : Rapport d'évaluation d'unité de recherche
N° S2PUR150008293

Monsieur le Directeur,

Vous m'avez transmis le 13 mai dernier, le rapport d'évaluation de l'unité de recherche « Tumor Immunology and Immunotherapy », N° S2PUR150008293 et je vous en remercie.

L'université se réjouit de l'appréciation portée par le Comité sur cette unité et prend bonne note de ses suggestions.

Madame Laurence Zitvogel, directrice de l'unité, n'a pas souhaité émettre d'observation générale sur le rapport.

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


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