



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

Section des Unités de recherche

AERES report on the canceropole

Canceropole GO

From the

Institut du Cancer

February 2011



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

Section des Unités de recherche

# AERES report on the canceropole

Canceropole GO

From the

Institut du Cancer

Le Président  
de l'AERES

Jean-François Dhainaut

Section des unités  
de recherche

Le Directeur

Pierre Glorieux

February 2011



# Canceropole

Name of the research unit: Cancéropole GO

Name of the director: M. BATAILLE

## Members of the review committee

Committee chairman :

M. Paolo DELLABONA, San Raffaele Scientific Institute, Milan, Italy

Other committee members :

M. Cristiano FERLINI, Danbury Hospital Research Institute, Danbury, USA

M. François FUKS, Laboratoire d'Epigénétique du Cancer, Bruxelles, Belgique

## Observers

AERES scientific advisor :

M. Nicolas GLAICHENHAUS

INCa representatives :

M. Fabien CALVO

Ms. Véronique ATGER



# Report

## 1 • Introduction

- **History and geographical localization of the canceropole, and brief presentation of its field and scientific activities**

The Canceropole GO originated in 2003 from the inventory of cancer oriented research based in the regions of Western France (Brittany, Centre, Pays de la Loire and Poitou-Charentes). The structures involved are scattered in 6 locations: Angers, Brest, Nantes, Poitiers, Rennes, Tours-Orleans. It is focused on 6 research themes : Tumor targeting and radiotherapy network, Natural sea products in cancer treatment, Immunotherapies, Integrated biology of cancers (pharmaco genomics, pharmaco genetics), Cancer stem cell, Clinical transfer/Clinical Research Platform and 2 supporting platforms: Functional imaging, Tumor repository.

- **Management team**

The Scientific Director and the management team seem to be made of experienced people in their respective field of research or clinical activity.

## 2 • Overall appreciation on the Canceropole

- **Summary**

The reviewers appreciate the efforts of the managing team of this Canceropole towards the improvement of the network performance and the involvement as pervasive as possible of the scientists working in the region. Nevertheless, the reviewers admit of having had quite some difficulties to identify in the written report all the information required to address the revision points raised by AERES, because the report was based on an enormous, dishomogenous (from theme to theme) and somewhat confusing input of data. That said, this Canceropole comprises a large network of scientists and clinicians involved in cancer research and experimental cancer therapy. It covers all the major and updated research areas in the field, with several internationally recognized participants. The scientific output is generally solid with several publications in top notch journals. There is a strong potential for collaborations between pre-clinical and clinical cancer research and efforts have clearly been done in this direction. Research themes in the Canceropole have also the potential to attract interest from industry. Overall, this Canceropole was not very effective.

- **Strengths and opportunities**

- High potential of each separated axis including those dealing with chemistry. The chemical screening from marine-derived products is promising, also in terms of attraction for industrial development. The overall potential is high;

- Enormous potential for cancer-related immunotherapy and tumor-targeting projects;

- The high potential of the cancer stem cell theme integrated in the tumor targeting and chemistry projects;

- The decision to merge the normal and the cancer stem cell projects in a single axis;



- The opportunity to exploit the uniqueness of the marine-derived products.

- **Weaknesses and threats**

- Lack of strategic vision;
- Geographical dispersion;
- Excessive scientific dispersion and lack of focus;
- Very little capability to convey discoveries into integrated and innovative clinical projects ;
- Surprising absence of internationally visible scientists in the Canceropole activities;
- Limited number of international collaborations and no strategic plan to increase them;

- Although in principle commendable, the attempt to involve the largest possible number of cancer oriented scientists in the canceropole GO could also pose a threat to the efficacy of the organization, unless extremely carefully managed. The impression, after reading the report, is in fact an overall lack of a clear strategic vision, which is strengthened by the direct comparison with other CP (for instance IdF, CLARA, PACA). A major weakness for the principle GO seems to derive from an excessive dispersion, or lack of focus, in the proposed pre-clinical and, especially, translational activities. The various Themes of research are each strong, yet they would benefit from a clearer identification of limited number of « Canceropole-specific » cancer pathologies (GBM, melanoma, mesothelioma, hematological malignancies seem to dominate in the report) onto which target the efforts of pre-defined, high priority and possibly integrated/combined therapeutic projects.

- **Recommendations to the head of the Canceropole**

- Improve the management;
- Develop a strategic vision including dedicated programs to encourage younger scientists to participate to Canceropole activities;
- Increase the connections with other Canceropoles including the IdF Canceropole for axis 1 especially.

### 3 • Specific comments

- **Contribution of the Canceropole to the structuration of the research at the local level**

*Appreciation on the initiatives aiming at a better use of biological resources (existence of a data base for biological resources, number of samples, quality control...):* The canceropole GO has put in place a supervised Tumor Repository that might prove very useful for research, clinical activities and, within the appropriate ethical constraints, also for the partnerships with industries.

*Appreciation on the quality of the partnership between the Canceropole and the scientific and industrial clusters :* The Canceropole has signed collaboration contracts with Merck, Serono, Amgen and Roche. The Canceropole is also taking part in a program to assist and support scientists in the industrial development of translational research products (MATWIN : Maturation & Accelerated Translation With Industry). Two (out of seven) projects have passed the steering committee and are in the process to be assessed by MATWIN. A collaboration with the Atlantic Biotherapies centre is being actively pursued to facilitate R&D in the canceropole GO.

*Appreciation on the quality of the partnership between the Canceropole and the local funded agencies (conseil général, conseil régional, universités) :* Fruitful relationships seem to undergo between the Canceropoles and the



local funding agencies. Regional councils of Brittany, Centre and Pays de la Loire fund directly the canceropole GO activities.

- **Appreciation on the strategy, management and life of the Canceropole**

*Relevance of the Canceropole's organization, quality of the management* : The organization of canceropole GO seem to suffer from the lack of an overall clear strategic vision, even though each single managing person is well qualified and experienced.

*Relevance of the Canceropole's communication policy* : The communication policy of the canceropole GO looks pretty standard.

*Relevance of the initiatives aiming at the scientific animation* : The canceropole GO organizes series of meetings and workshops internal to the participants as well as open meetings with external participants. Both communication and animation could benefit from annual "scientific retreats" of each research Theme or ad hoc combined Themes, in the presence of the Scientific Director and the managing team, aiming both at verifying the progression towards the defined strategic objectives and defining possible new areas of cooperation.

- **Appreciation on the project**

*Relevance of the project according the INCa priority 1 (structuration of the research at the local level)* : The cancer research in the region has been structured by the action of the canceropole GO. The problem is the strategic vision of this structuration.

*Relevance of the project according the INCa priority 2 (differences et facteurs de risque)* : A web site posting all available clinical trials has been created and implemented to inform patients from the territory about their newest therapeutical opportunities. In addition, the Experience, ethics and practice Theme seems to quite aggressively address the problem of inequalities and the factors of environmental and behavioural risk by finalizing 14 studies.

*Relevance of the project according the INCa priority 3 (valorisation)* : This canceropole has been quite successful in fostering and/or supporting the development of industrial spin-off from the affiliated research teams. Particular active from this point of view appear the Themes Use of marine-derived products in cancer treatment and Integrative biology of cancer.

*Relevance of the project according the INCa priority 4 (europe)* : Several research groups working in the canceropole GO were funded by EC grants.

- **Appreciation on the quality of SWOT analysis**

There is an overall agreement with the SWOT analysis of pros and cons of the canceropole GO. As a specific comment, again, any recruitment of new teams in the canceropole GO, or investments of the like, should be underpinned by a specific strategic design.



## 4 • Appreciation theme by theme

- Title of the theme: Tumor targeting and radiotherapy network
- Name of the theme leader: M. Jacques BARBET

Number of teams involved in this theme in 2007: 15.

Number of teams involved in this theme in 2010: 21.

- Appreciation on the results

*Appreciation on the quality of the 3 most important discoveries identified by the Canceropole (originality, quality of publications,...) :* Specific information not found in the report. The general lists of publications concerning this Theme shows a solid scientific production.

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time :* There were 48 projects submitted between 2007-2010 of which 14 funded (30%). The funding rate shows a somewhat a decreasing trend from 2007 to 2010.

- Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects

*Appreciation on the number and the quality of the seminars and conferences :* This Theme is active in terms of distribution of information (workshops, seminars).

*Existence of fruitful collaborations between Canceropole teams that have resulted in co-authored publications :* Information not specified in the report.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field :* There are several active collaborations between participant of this Theme and scientists from other fields.

*Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs :* Not clear from report.

- Conclusion :

- Summary

Overall good project.

- Strengths and opportunities

Actively producing reagents for diagnosis and therapy.

- Weaknesses and threats

Not completely integrated with immunotherapy or integrated cancer biology at the level or pre-clinical research development. It is also advisable to define a cancer stem/initiating cell targeting project.



— Recommendations

Improve integration with other Themes to try developing novel and original integrated tumor targeting approaches with molecular and cellular anti-tumor effectors.

- **Title of the theme: Immunotherapies**
- **Name of the theme leader: M. Yves DELNESTE**

Number of teams involved in this theme in 2007: not existing (Cell Therapy).

Number of teams involved in this theme in 2010: 32.

- **Appreciation on the results**

*Appreciation on the quality of the 3 most important discoveries identified by the Canceropole (originality, quality of publications,..)* : This is possibly the area of activity in this Canceropole with the strongest expertise and international visibility. The scientific production originated by this theme is of very high quality.

*Concrete results of the research activity and socio-economic partnerships* : Two start-up companies created from groups working in this Theme.

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time* : This Theme has 13 projects funded by INCA in 2007-2010.

- **Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects**

*Appreciation on the number and the quality of the seminars and conferences* : There are meetings scheduled for thematic working groups. An international symposium was organized in December 2010.

*Existence of fruitful collaborations between Canceropole teams that have resulted in co-authored publications* : Not evident from report.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field* : There are plans to reinforce the interactions with research teams working in transplantation immunology, which addresses from a opposite perspectives the very same scientific problems of tumor immunology: namely tolerance induction and breaking.

*Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs* : Not evident from the report.

- **Conclusion :**

— Summary

Very strong and well structured theme of research.

— Strengths and opportunities

Natural propensity to develop innovative experimental treatment for cancer. High quality and expertises of the teams involved in this Theme.





— Weaknesses and threats

This Theme has not yet included (apparently) a team developing active (vaccine) immunotherapy of cancer. There are still limited interactions with Tumor targeting and radiotherapy Theme, which could be result in original therapeutic approaches.

— Recommendations

Invest on this Theme by supporting the development of clinical studies/trials and fostering the interaction with other Themes, such as Tumor targeting and radiotherapy, which can synergize in the development of novel cancer treatments. A cancer stem/initiating cell immunotherapy project may also be envisaged.

- **Title of the theme: Use of marine-derived products in cancer treatments**
- **Name of the theme leader: M. Philippe BOUGNOUX**

Number of teams involved in this theme in 2007: 25.

Number of teams involved in this theme in 2010: 28.

- **Appreciation on the results**

*Appreciation on the quality of the 3 most important discoveries identified by the Canceropole (originality, quality of publications,...)* : The publications that concern this Theme are on solid journals.

*Concrete results of the research activity and socio-economic partnerships (if relevant)* : The research activity in this theme has delivered lead chemicals for further development and partnerships with industry and/or promoted industrial development (ManRos).

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time* : There are 2 projects funded by INCA in 2007-2010.

- **Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects**

*Appreciation on the number and the quality of the seminars and conferences* : Not evident from report.

*Existence of fruitful collaborations between Canceropole teams that have resulted in co-authored publications* : Possible, not evident from report.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field* : There are interactions with scientists from other fields, although this is not clearly specified by the report.

*Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs* : This Theme is quite succesfull in the participation to European calls (three projects awarded).

- **Conclusion :**

— Summary

It is certainly an original, possibly the most original, area of interest of this Canceropole.



– Strengths and opportunities

Very effective organization of in vitro and in vivo screening platforms. This Theme offers the possibilities to interact with the other Themes in the canceropole GO to develop original compounds for innovative therapeutic approaches.

– Weaknesses and threats

A more focused screening strategy and a deeper integration in the biology screening could profit from the unicity of the chemical diversities coming from the sea world. The Reviewers believe that the strategy of this Theme should be updated on focused targets. The activities of optimisation of the screening should be enhanced by an integrated center of computational biology. In the absence of an updated strategy this Theme runs the risk to become not competitive with big Pharma and other academic centers.

– Recommendations

Carefully identify the scientific niches where to address the activity of this high potential Theme in order to deliver « orphan » products that could be really attractive for pharma industry investments. Foster and support maximal interactions with Tumor targeting and radiotherapy and Immunotherapies Themes to identifies possible new way to approach the development of integrated cancer therapy. Include Cancer stem/initiating cells in the screening platforms for anti-cancer drugs. Promote utilisation of the screening platforms available in Canceropole IDF to maximise the usefulness of the generated library of compounds.

- **Title of the theme: Integrated biology of cancers**
- **Name of the theme leader: M. Alain MOREL and Ms. Marina DENYSET**

Number of teams involved in this theme in 2007:

Number of teams involved in this theme in 2010:

- **Appreciation on the results**

*Concrete results of the research activity and socio-economic partnerships (if relevant) :* The Theme has had an apparent substantial impact in promoting industrial partnerships and spin-off development.

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time :* The success funding rate of this Theme with INCA projects is 20% (75 submitted, 15 funded). There seem to be a slight worsening of the funding rate going from 2007 to 2010.

- **Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects**

*Appreciation on the number and the quality of the seminars and conferences :* The Theme has an active dissemination activity of good quality.

*Existence of fruitful collaborations between Canceropole teams that have resulted in co-authored publications :* Difficult to extrapolate from report.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field :* Effort are made to prompt collaborations between the participants of this Theme and scientists from other Themes.

*Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs :* Difficult to extrapolate from report.



- **Conclusion :**

- Summary

Very active and well productive Theme in terms of scientific output.

- Strengths and opportunities

The Theme relies on a relevant repository of tumor samples and on the availability of large patient cohorts already stratified for clinical responses.

- Weaknesses and threats

Until 2009, this Theme has looked very much like an « allinclusive » research, completely devoid of strategic vision and priorities. It seems that since 2009 some limits were introduced to canalize the « omics » activity towards more defined strategic goals.

- Recommendations

Apply the « omics » expertise and platforms also to more integrated approaches involving the activities of the other Themes, for instance in the evaluation of the response to patients to various experimental therapeutic approaches conceived at the canceropole GO.

- **Title of the theme: experience, ethics and practices**

- **Name of the theme leaders: M. Philippe COLOMBA and Ms. Sylvène RENOUD**

Number of teams involved in this theme in 2007: 7.

Number of teams involved in this theme in 2010: 18.

- **Appreciation on the results**

*Appreciation on the quality of the 3 most important discoveries identified by the Canceropole (originality, quality of publications,...) :* The teams involved in this area published 23 papers, although it was not reported where.

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time :* Two INCa projects were obtained in 2005 and 2008. Not clear out of many projects submitted.

- **Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects**

*Appreciation on the number and the quality of the seminars and conferences :* This seems to be a very active Theme in terms of communication and it has organized a number of seminars on the thematic.

*Existence of fruitful collaborations between Canceropole teams that have resulted in co-authored publications :* Not found.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field :* There is a more than satisfactory interaction with other Themes of research and, especially, clinicians (for instance Oncopediatrics).

*Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs :* Not highlighted in the report.



- **Conclusion :**

- Summary

Very recent although quite dynamic Theme.

- Strengths and opportunities

An original view of the objectives to achieve.

- Weaknesses and threats

For the time being, no particular weaknesses are disclosed.

- Recommendations

Try best integration on few and well defined strategic objectives with the other Themes.

- **Title of the theme: Stem cell and cancer**
- **Name of the theme leader: Ms Francoise VALLETTE, Ms Elise PETIT-RODAT**

Number of teams involved in this theme in 2007:

Number of teams involved in this theme in 2010: 18.

- **Appreciation on the results**

*Appreciation on the quality of the 3 most important discoveries identified by the Canceropole (originality, quality of publications,...) :* No publications shown in the report.

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time :* Not shown in the report.

- **Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects**

*Appreciation on the number and the quality of the seminars and conferences :* Very active and well organized Theme with seminars and meetings.

*Existence of fruitful collaborations between Canceropole teams that have resulted in co-authored publications :* Co-authored publications are being submitted.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field :* There are already contacts with scientists in other fields and more are planned.

*Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs :* The Theme has just begun in 2009 and its teams did not participate yet to european calls.

- **Conclusion :**

- Summary

Recent, active and well organized Theme.



- Strengths and opportunities

The strengths of this Theme may reside both in the interactions with other Themes as well as in its intrinsic autonomous value. The fact to have combined the study of normal and cancer stem cells in a single Theme is appreciated by the Reviewers.

- Weaknesses and threats

Danger of remain isolated from the other better established Themes.

- Recommendations

This Theme has potential to develop well in interesting areas of translational medicine. It must be supported with resources and helped to integrate with the other Themes. Exploit the cancer stem/initiating cells in the screenings of chemicals from marine-derived products.



## **Response to AERES report on the Cancéropôle GO (CGO)**

### **Canceropole Grand Ouest**

Scientific director : Pr FR BATAILLE

### **Members of the review committee**

Committee chairman :

M. Paolo DELLABONA, San Raffaele Scientific Institute, Milan, Italy

Other committee members :

M. Cristiano FERLINI, Danbury Hospital Research Institute, Danbury, USA

M. François FUKS, Laboratoire d'Epigénétique du Cancer, Bruxelles, Belgique

### **Observers**

AERES scientific advisor :

M. Nicolas GLAICHENHAUS

INCa representatives :

Pr. Fabien CALVO

Ms. Véronique ATGER

## 1) General comments concerning the report.

First, we would like to thank the experts for their times and the in-depth analysis of the CGO activities.

However, we feel that some of the negative points we found in their report are not reflecting the truth, probably because some points were lacking in our written and oral documents.

### 1.1) CGO's governance and management.

We must disagree with the analysis.

Since 2003 the scientific targets of CGO have largely been remodeled (see slides N° 11 of the presentation), some have disappeared, others have emerged (Social sciences, stem cells, integrated biology of cancer, gliomas, immunotherapy). Incidentally, all these new scientific targets of CGO have been well appreciated by the experts. These evolutions have been suggested and monitored by members of the CGO themselves under the supervision of Professors MEFLAH and BATAILLE, respectively former and actual director of CGO. We feel thus that the governance has been strong albeit collective. Furthermore, as detailed in our document, the President and the scientific director have visited all the six major sites of the CGO on a one day brainstorming session basis, have attended the major brainstorming sessions of each research theme and organized and attended the annual two days scientific sessions of the CGO to review and discuss all the research teams of the CGO.

We are thus surprised by the ambiguity of the last sentence of the summary :...”overall, this Cancéropôle was not very effective” found at the end of the summary, summary which was a generally fair introduction.

Here are our answers to some other points :

### 1.2) Geographical dispersion.

The perimeter of the CGO was defined at the time by INCa upon the establishment of Cancéropôles (see the original text of 2003 <sup>1</sup>). This dispersion is intrinsic to our territory which is vast but comparable in terms of scientific and medical populations with the other Cancéropôles. Note that this geography is similar (for the same reasons) for the DIRC (clinical organization), the league against cancer and the western France biotech cluster Atlanpole biotherapy. However, we understand that the AERES experts, as foreigners, feel that this is an intrinsic weakness. Somehow the CGO has been instrumental in reducing the size of this “vast area” **by its strategic vision**. In few years the CGO was able to create among researchers and clinicians a real sense of community and belonging to a territory. This is illustrated in routine works of the Cancéropôle but also experienced by the scientific director at every CGO seminars thematic work. For example, the towns of Orleans and Tours (Région Centre) totally ignored each other before the CGO (2003) and even had a non-constructive competition within their own Region. Since then, and thanks to CGO, the 2 cities have real scientific collaborations in terms of research against cancer and other plans now, even economic ...

Does INCa request that each city has its own Cancéropôle specificity ? That is not in the specifications of Cancéropôles or we would escape.

---

<sup>1</sup> « promouvoir l'émergence des « Cancéropôles » établies à l'échelle d'une région ou d'un groupe de régions et donner un nouvel élan à l'effort de recherche dans le domaine de la lutte contre le cancer. Les Cancéropôles ont vocation à développer la coordination opérationnelle de projets mobilisant des équipes de recherche labellisées, des services de soins orientés vers l'innovation et des plates-formes technologiques mutualisées. ». Appel à propositions 2003 Emergence de Cancéropôles

### **1.3) Science dispersion.**

Obviously, this is a consequence of the geographical dispersion. The dispersion was quite high at the beginning and decreased over time. What was a weakness became a strength inherent in the GO. To give an example, many laboratories now work on gliomas and thus have shifted their previous work with the help and the direction of the CGO. By the way, Gliomas is a tumor of interest for CGO, and this particular and important point, a major token of the CGO governance, is not mentioned in the report. We can say that apart from the social sciences, the common axis is therapeutic targeting, that in particular includes marine-derived products theme.

This represents an overall consistency, which is in contradiction with your criticisms.

### **1.4) Weakness of translational research.**

As opposed to what was noted by the experts, we think that there is a real consistency of our translational research activities which has been outlined in a specific research theme (Integrated biology of cancers) which has been well evaluated. As such we would like to remind you of the initial specifications of Cancéropôles (see the text in <sup>2</sup>). We know there is since 2010 a specification for SIRIC. This is totally separate from Cancéropôles and we fully integrated

### **1.5) Lack of strategic vision.**

The initial strategy of CGO was to bring together basic and clinical research teams from a vast territory (see the text in <sup>2</sup>). As such, the CGO has fully played its role in reducing the barriers between regions, university hospitals, universities and cities. Maybe we should have shown this in more details. However, this point (i.e. geographical dispersion and the dispersion of topics) is now fully addressed by the INCa/SIRIC projects, which are designed to work teams at a geographical site on very specific topics (with tumors of interest) for the dissemination of knowledge for both health professionals and patients. This has been discussed by members of the CGO and it has been decided that only one SIRIC project will be presented by the CGO.

We think that this is a proof of our good governance and of a real strategic vision.

### **1.6) Lack of international scientists.**

Since the beginning of its establishment, CGO wished to emphasize, by its strategic vision on the subject and not on persons. Many researchers of the CGO have a high international recognition and several reach a h-index superior to 60.

Nonetheless, we are fully aware that Cancéropôles reviewed by the same panel of experts (i.e. CLARA, IDF and PACA) with a more critical mass of researchers have more visible personalities. Once again, the geography/ history could be accounted for the lack of international visible persons. Keep in mind that our strategic views favour collective achievements rather than individual ones. We are aware that it might not be politically correct, at least for the moment.

---

<sup>2</sup> « promouvoir l'émergence des « Cancéropôles » établies à l'échelle d'une région ou d'un groupe de régions et donner un nouvel élan à l'effort de recherche dans le domaine de la lutte contre le cancer. Les Cancéropôles ont vocation à développer la coordination opérationnelle de projets mobilisant des équipes de recherche labellisées, des services de soins orientés vers l'innovation et des plates-formes technologiques mutualisées. ». Appel à propositions 2003 Emergence de Cancéropôles.



## 2) Specific comments theme by theme.

### 2.1) Title of the theme : Tumor targeting and radiotherapy network

Name of the theme leader : M. Jacques BARBET - And co-worker Ms Françoise LEOST

*Number of teams involved in this theme in 2007: 23 (15 preclinical research teams and 8 clinical research teams)*

*Number of teams involved in this theme in 2010: 37 (21 preclinical research teams and 16 clinical research teams)*

#### ***Appreciation on the results***

*Appreciation on the quality of the 3 most important discoveries identified by the Cancéropôle (originality, quality of publications,..) : Specific information not found in the report. The general lists of publications concerning this Theme shows a solid scientific production.*

We should have described only 3 "most important discoveries". In fact we have detailed 5 major progresses that have judged significant for the 3 reference years:

1. Preclinical and clinical advances on a new rhenium-188 complex (rhenium-188 lipiodol in phase I clinical study, efficacy of rhenium-188 nanocapsules in the treatment of glioblastoma in rats)
2. Advances in the preclinical alpha-immunotherapy of multiple myeloma: efficacy of a bismuth-213-labelled anti-CD138 antibody in a mouse syngeneic model of multiple myeloma.
3. Targeting of bone resorption in primary bone tumours (treatment of osteosarcoma in mice using an osteoprotegerin biopolymer, validation of gene transfer in experimental models of primary bone tumours)
4. Feasibility of aerosol therapy with therapeutic monoclonal antibodies (cetuximab)
5. Patient-specific dosimetry in nuclear medicine (standardization of procedures in the clinic)

*Appreciation on the number of projects that have been submitted and funded by INCa and on the evolution of these numbers with time : There were 48 projects submitted between 2007-2010 of which 14 funded (30%). The funding rate shows a somewhat a decreasing trend from 2007 to 2010.*

We have discussed the difficulty for our multidisciplinary project to be evaluated within the INCa calls for tender. The success rate in ANR or European calls is comparably better.

#### ***Relevance and impact of the initiatives aiming at the scientific animation and at the emergence of cutting edge projects***

*Appreciation on the number and the quality of the seminars and conferences : This Theme is active in terms of distribution of information (workshops, seminars).*

With respect to the particular efforts brought by this Theme to the scientific animation and to the success of its initiatives, this low-key appreciation is really fair.

To summarize, we organize each year one internal scientific meeting, one thematic workshop open at the national level within the Annual Meeting of the Nantes University, one three-day international thematic workshop (Berder Island) that brings together young scientists from several countries and this Theme is involved each year in a decisive manner in the organization of international symposia (Nuclear Medicine Tomorrow in 2008, the 1st TARCC-TRT International Workshop on Targeted Radionuclide Therapy in 2009 and the international workshop "Is there a future for Innovative PET Radionuclides  $^{64}\text{Cu}$ ,  $^{68}\text{Ga}$ ,  $^{89}\text{Zr}$  and  $^{44}\text{Sc}$  ?" in 2010. In 2011, there will be no international symposium because of the AERES evaluation, but in 2012, this Theme has managed to have the European Society of Radiopharmacy and Radiopharmaceuticals 2012 symposium organized in Nantes.

*Existence of fruitful collaborations between Cancéropôle teams that have resulted in co-authored publications : Information not specified in the report.*

This information was given in the report and repeated during the presentation: for the 3-period, there were 26 co-authored publications.

*Appreciation on ability of the participants to the theme to interact fruitfully with scientists from other field : There are several active collaborations between participant of this Theme and scientists from other fields.*

This is true, but again, this appreciation does not reflect the highly multidisciplinary activity of this Theme (physics, chemistry, biology, medicine, computer science) that makes both its originality and its difficulty.

*Appreciation on the ability of the involved teams to participate to Cancer-related European calls and programs : Not clear from report.*

Indeed, we made the mistake not to insist on this point. European collaborations were only mentioned in an annex that was not included in the final report. In a non-exhaustive manner, for this Theme, we may recall:

EC FP7 HEALTH-2007

TARCC « Targeting Alpha-particle emitting Radionuclides to Combat Cancer », (2007-2010), Partners: Inserm, Nantes, Technische Universität München; Medizinische Hochschule Hannover; Göteborg University; University Medical Centre Ljubljana; Centre National de la Recherche Scientifique, Nantes; Joint Research Centre-Institute for Transuranium Elements; Ion Beam Applications SA; University Hospital of Freiburg; Inserm Transfert, Coordinator: Jacques Barbet, Inserm, Nantes.

ITEA 2: Information Technology for European Advancement

MEDIATE ("Patient Friendly Medical Diagnosis & Treatment") (06/2010-06/2013), Partners: LaTIM Brest France, Philips Healthcare Pays Bas, BARCO Belgium, CEA France, Ansys France, LTSI Rennes France, Institut Telecom France, ATOS Origin Spain, Philips Medisys; SQI France, Endocontrol France, Coordinator: Rob Smeets, Philips Healthcare

EC FP7 HEALTH-2009-1.2.4

ENVISION ("European Novel Imaging Systems for ION therapy") (01/2010 – 12/2013), Partners: CNRS IN2P3, Brest, ETOILE, INFN Italy, CSIC Spain, CERN, Oncoray Germany, Gent University, Belgium, Maastrro Clinics, The Netherlands, GSI Germany, IBA Belgium, SIEMENS, Germany, Coordinator: CERN

**Conclusion :**

*Summary*

*Overall good project.*

Thank-you

*Strengths and opportunities*

*Actively producing reagents for diagnosis and therapy.*

*Yes, but, honestly, if this is all what remains in mind...*

*Weaknesses and threats*

*Not completely integrated with immunotherapy or integrated cancer biology at the level or pre-clinical research development. It is also advisable to define a cancer stem/initiating cell targeting project.*

The interest of a "complete integration" with immunotherapy or integrated cancer biology is not clear within the strategy of this Theme. A cancer stem/initiating cell targeting project is far more interesting and is being discussed within this Theme. Unfortunately we have not yet entirely identified a realistic and not too naïve approach, although alpha-emitting radionuclides are very interesting in this context. We resisted presenting a premature project that would have but too easily criticized. A dialog is open with the other Themes, particularly with Stem cell and cancer.

*Recommendations*

*Improve integration with other Themes to try developing novel and original integrated tumor targeting approaches with molecular and cellular anti-tumor effectors.*

One of the strengths of the "Tumor Targeting and Radiotherapies" Theme is the presence of internationally recognized laboratories and clinical departments in nuclear medicine and medical physics. The coherence of opening the Theme to external beam radiotherapy was explained in detail. These approaches distinguish this Theme with respect to what is done in other Cancéropôles and, up to now, this strategy has been positively received. Translational research in "radiotherapies", both targeted and external, will remain a strong part of the Theme. Targeting molecular effectors is not excluded and is or was the object of projects within this Theme. However targeting cellular effectors, a research domain developed in many other places, has not been considered. This approach could have been developed by another Theme of the Cancéropôle Grand Ouest that was recently discontinued.

It remains rather surprising that none of the words "radiotherapy", "radionuclide" or "Nuclear Medicine" has been used in this evaluation report.

**2.2) Title of the theme : Immunotherapies**

**Name of the theme leader : M. Yves DELNESTE - And co-worker : Ms Sylvène RENOUD**

We thank the AERES committee for the positive evaluation of the theme "Immunotherapies" and for the constructive comments and recommendations.

We will take into account the overall evaluation, which is going to be useful for the future strategy of the theme.

Please find hereafter the responses to some specific comments:

1. *“Existence of fruitful collaborations between Cancéropôle teams that have resulted in co-authored publications: Not evident from report.”*

Data on this specific task was not detailed in the written report. To date, collaborations between teams of this theme have already generated 11 co-authored publications (8 scientific articles and 3 reviews). As examples, we can mention the following publications:

- in topic 1, a publication by teams working in Nantes, Rennes and Brest (J Gene Med. 2008;10:628-36) and a publication by teams working in Angers, Nantes and Brest (Biomaterials. 2010;31:321-9),
- in topic 2, a publication by teams working in Nantes and Rennes (Int J Cancer. 2009;125:374-80),
- in topic 3, a publication by teams working in Nantes and Tours (Blood. 2006;107:4669-77).

We can also mention a publication by teams of topic 1 and of the emerging topic “Cytokines” (Eur Cytokine Netw. 2008;19:166-75) and a publication by teams of topics 1 and 2 (Clin Cancer Res. 2006;12:7380-8). At this time, the limited number of publications may result from the fact that this theme was initiated in 2008.

We agree with the committee’s comment that we have to promote collaborative publications. Based on the recent meetings; we are confident that co-authored articles will emerge from this theme.

2. *“Appreciation on the ability of the involved teams to participate to Cancer-related european calls and programs : Not evident from the report”*

Data on this specific task was not detailed in the written report. Three teams were integrated in cancer-related European programs, two in the theme “Immunotherapies” (CHILDHOPE, 2006-2009; Integrated research project “Cancer Immunotherapy”, 2006-2010) and one in the emerging topic “Cytokines” (program COST “MPN & MPNr EuroNet”, 2010-2014).

3. *“This Theme has not yet included (apparently) a team developing active (vaccine) immunotherapy of cancer”*

We agree with this comment as integrating teams involved in clinical trials may allow refining strategies. Clinicians involved in cell-based clinical trials have been already integrated in this theme. Clinicians are also integrated in the topic “Therapeutic mAbs”. As mentioned during the presentation, we have recently initiated discussion with teams involved in cancer vaccine trials.

Anyway, and as underlined by the experts, we have to strengthen the integration of clinicians involved in immune-based clinical trials.

4. *“There are still limited interactions with Tumor targeting and radiotherapy Theme, which could be result in original therapeutic approaches” and “A cancer stem/initiating cell immunotherapy project may also be envisaged”*

We agree with this specific comment. Collaborative projects with the theme “Cancer and stem cell” have been already initiated, especially in glioblastoma. Collaborations with the “Tumor targeting and radiotherapy” theme should be fruitful.

### **2.3) Title of the theme : Use of marine-derived products in cancer treatments**

**Name of the theme leader : M. Philippe BOUGNOUX** - And co-worker : Ms Aurore DOUAUD

The originality of the axis has been recognized by the experts. There is a number of scientific niches we plan to capitalize on. These are exemplified by the interactions within CGO, as documented with 14 publications co-authored by teams belonging to distinct disciplines (chemistry, cell biology, preclinical models). We acknowledge the recommendations. A focused working group will determine the strategic direction of the axis and modalities to set up, in order to implement the tactical changes that have been proposed.

### **2.4) Title of the theme : Integrated biology of cancers**

**Name of the theme leader : M. Alain MOREL** - And co-worker Ms. Marina DENYSET

We agree with the experts that collaborations between Cancéropôle were not detailed in the report. We should notice that our priority during the past years was to mobilize the collaborations between GO teams and now as it is suggested by the experts, collaboration between Cancéropôles must be a goal for the next years.

Concerning the participation to cancer-european calls and programs, CGO was not involved directly in these actions but numerous teams in GO are involved to european programs as coordinator or associates.

To improve our reorganisation, immediate actions will be to identify the specializations for each omics plate-form in order to clarify the service that will be done for the patients and clinicians. In conclusion, we have appreciated the recommendations made by the experts which will be very useful to improve our development.

### **2.5) Title of the theme : experience, ethics and practices**

**Name of the theme leader : M. Philippe COLOMBAT** - And co-worker Ms. Sylvène RENOUD

The reviewers did not note any particular weakness. They only recommend a better integration of few and strategic objectives with other themes. We will consider these recommendations.

**2.6) Title of the theme : Stem cell and cancer**

**Name of the theme leader : M Francois VALLETTE - And co-worker Ms Elise PETIT-RODAT**

We thank the experts for their encouraging remarks. We agree on the necessity to collaborate with the other themes and several projects are underway in particular with the “tumor targeting and radiotherapy” and the “immunotherapies” themes.

**2.7) Title of the theme : Glioma**

**Name of the theme leader : M. Mario CAMPONE - And co-worker Ms. Marina DENISET**

No comment was made on gliomas. This is very disappointed for us, since we consider gliomas a strong tumor of interest of GO. This is also difficult to understand since a reviewers criticisms was not to detail our tumor of interest.

**Pr FR BATAILLE**

Scientific Director of Cancéropôle GO



—  
.