aviesan
alliance nationale
pour les sciences de la vie et de la santé

ITMO Cancer

The PMSI Programme

Physics, Mathematics and Engineering Sciences

Applied to Cancer

Ex Post Analysis
2011-2017

(May 2018)

Introduction

In the frame of the 2nd and 3rd Cancer Plans, the Multi-Organization Thematic Institute (ITMO) Cancer of the Alliance for Life Sciences and Health (Aviesan) is since 2011 responsible for the thematic calls for projects to support emerging research domains. These funding instruments, whose operational management falls to Inserm, are launched in the frame of the research part of the national Cancer Plan, which is coordinated by the National Cancer Institute (INCa).

In accordance with the recommendations of the INCa's international scientific advisory board and the third Cancer Plan objectives, a discussion about programme evaluations has started at the national level.

In parallel, ITMO Cancer-Aviesan started assessments of its own programmes for which a sufficient hindsight is possible. A generic analysis grid that can be used for all programmes has been implemented to achieve this. This analysis methodology can be slightly adapted to the specificities of the different calls for projects.

The ex post analyses of ITMO Cancer are fulfilling the following objectives:

- To determine if a funding programme has reached its objectives and to which cancer plan objectives it contributed to;
- To gain insights on the impacts of the funding in terms of tools developed and scientific advances in oncology generated;
- To provide data and information allowing ITMO Cancer to implement evidence-based strategic steering of cancer research.

This document recapitulates the main elements of the ex post analysis of the PMSI Programme over the 2001-2017 period.

Elements Taken into Account in the Analyses

- Key figures of the number of projects submitted, success rate, average budget over time
- Analysis of the projects (*using the submitted information and the selection committee reports*):
  - ✓ PI profile: scientific domain*, experience on cancer, demographic data, affiliation;
  - ✓ Project types: domain (CSO categories), cancer type, duration of funding;
  - ✓ consortiums: partner number, domains*, type (industrial or academic, international);
  - ✓ main reasons of the rejection of non-selected project.
- Impact of the project *(based in the final reports and the discussions with PI during the restitution seminars)*:
  - ✓ Tools developed: diagnostics, therapeutics, follow up, uses by others;
  - ✓ Advances in knowledge: oncogenesis mechanisms, resistance pathways, potential therapeutic target identifications;
  - ✓ Socio-economical outcomes: manpower hired, patents, collaborations, PI career evolutions, leverage effects;
  - ✓ Communication: publications, oral or poster presentations in congresses, lay public reaching.

**Medicine/Clinical Research, Biology, Physics, Mathematics/Informatics/Engineering, Chemistry*

Context and Objectives of the Programme

The PMSI Programme was implemented by ITMO Cancer-Aviesan in collaboration with ITMO Health Technologies-Aviesan in the frame of the 2nd (2009-2013) and the 3rd (2014-2019) Cancer Plans:

- 2nd Cancer Plan: measure 1 "*To strengthen the means of multidisciplinary research*", including the following goals: "*Reinstate the importance of fundamental research by promoting originality and the importance of interactions between disciplinary fields*" and "*Accelerate the development and improve the quality of fundamental research tools*";

- 3rd Cancer Plan: objective 13 "*To provide means for an innovative research*", action 13.1 : "*To guarantee independence and creativity of research by insuring a funding over 50% of the whole INCA and ITMO Cancer calls for projects funding on fundamental research*", with the objective to "*foster within the calls for projects the interdisciplinary dynamics (biology, mathematics, bioinformatics, physics, chemistry, and social sciences and humanities)*".

The ambition of the PMSI Programme was to "*attract physicists, mathematicians and engineers in cancer research*", with a threefold objective:

- To foster an interdisciplinarity-oriented research community in France;
- To promote the development of diagnosis and therapeutic tools for cancer;
- To support the generation of knowledge on the fundamental processes of oncogenesis.

To achieve these goals, the call for projects has financed research projects at the interface of mathematics, physics and engineering sciences and oncology liable to improve the understanding, diagnosis or therapeutic management of cancer.

The scope of the Programme was defined by an ad hoc expert committee set by ITMO Cancer-Aviesan. The comparison of the scopes of PMSI Programme with those of the translational research (PRT-K) and the clinical research (PHRC-K) programmes managed by INCa within the frame of the cancer plan showed that PMSI is part of a research funding continuum covering the whole spectrum from fundamental to clinical research.

Scope of the PMSI Programme (Call 2017)

- External radiotherapy (beams, control and dosimetry), including hadrontherapy;
- Physical models of matter-particle interactions, including at the cellular level (micro- and nano-dosimetry);
- Imaging techniques linked to radiotherapies;
- Metabolic or vectorized radiotherapy for aspects concerning dosimetry;
- Novel physical approaches (acoutic waves, multiphotonic spectroscopy, and other new concepts) for tumour and cancer cell characterization;
- Novel physical approches for the therapeutic handling of cancers;
- Mathematical approaches allowing the modelling of the processes involved in the emergence and dissemination of cancers as well as therapeutic handling of cancers.

Ex Post Analysis of the Programme

KEY FIGURES

The call has generated an increasing interest from 2011 (50 submitted projects) to 2017 (almost 80 projects submitted), for a total of 108 funded projects over this period[1].

Main figures of the PMSI Programme

Projects 2011-2017
- 108 funded projects
- 95 PIs (22 % women)
- 247 partners
- M€ 30
- median age of PIs: 43 y.o.

Projects 2011-2013 (outcome analysis)*
- 51 projects
- 102 personnel hired (50 % post-doctoral fellows, 25 % engineers, 25 % graduate students)
- 23 international collaborations
- 3 interdisciplinary laboratories (including 2 international ones)
- 9 patents
- 2 start-ups
- 121 original articles

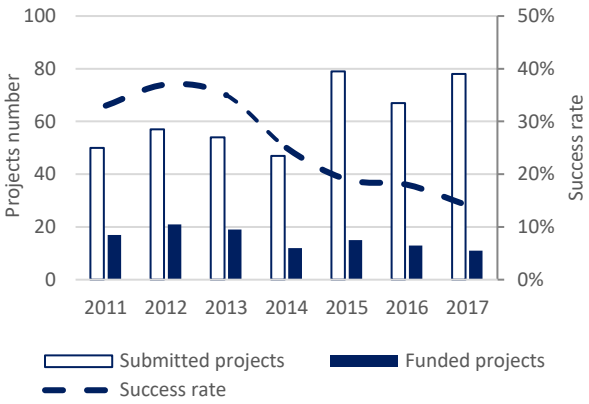
** as mentioned in the final reports*

During the same period, the average allocated budget has tripled (€450K in 2017 versus €150K in 2011), due to the increase in the project length (35 months in 2017 versus 21 months in 2011) and of the number of partners taking part (3,3 in 2017 versus 2,8 in 2011).

The total budget dedicated to the Programme has increased between 2011 (€3M) and 2015 (€5M), and remained stable since then.

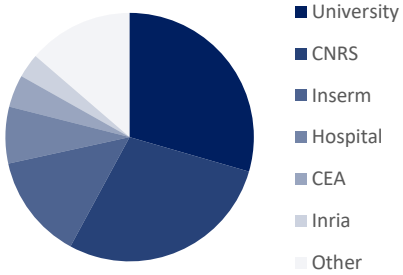
The success rate has therefore mechanically decreased from 33% in 2011 to 14% in 2017.

Submitted and funded projects, success rate



The majority of Aviesan founding members were present among the employers of the PI in the Programme: universities and CNRS (28% each), Inserm (14%), hospitals (7%), CEA (4%) and Inria (3%).

PI Employers

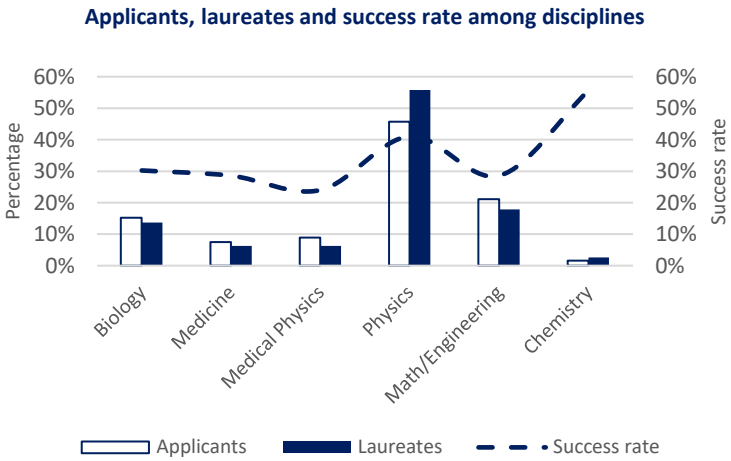


[1] This ex post analysis was made on 108 funded projects over the 2011-2017 period, except for the outcomes, that were analysed on 51 projects funded between 2011 and 2013 that were completed at the time of the analysis (May 2018).

TOWARDS A STRONGER MULTIDISCIPLINARY RESEARCH COMMUNITY ON CANCER

The first objective of the PMSI Programme was to foster the building of a community on cancer research that goes beyond discipline boundaries. The analysis has shed light on the Programme's ability to fulfil this objective.

➔ *Attractivity for Researcher Outside the Oncology Community*

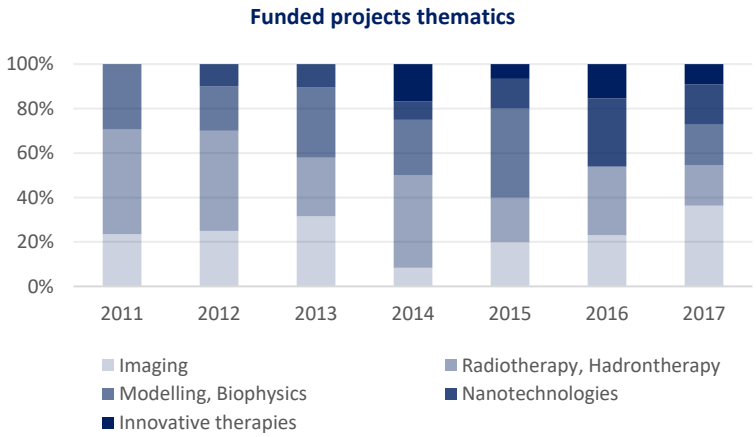


Among the 95 funded PI, almost half (44) did not have a large experience in the field of cancer at the submission. The Programme has therefore been a lever for researchers in a variety of scientific domains to add cancer to their research domains.

Physicists have been submitting in great number (46% of submitted projects), and had furthermore a higher success rate than the average (40 % *versus* 34%)[2].

➔ *Innovative Research in Different Fields*

Radiotherapy and hadrontherapy (including dosimetry) represent an important part of the projects (up to 50% during the first years of the Programme), in accordance with the scope of the call for projects. Imaging, modelling and biophysics were also present together with nanotechnologies that appeared in 2012.

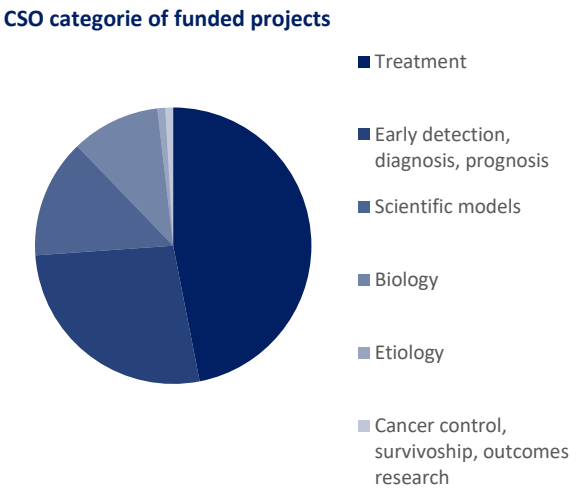


The new physics approaches were also a field that mobilised researchers as projects developing innovative therapies (electroporation-, optic-, acoustic- and plasma-based therapies) appeared in 2014, indicating that the Programme was instrumental to stimulate this type of research.

[2] The success rate of chemists is high, but their share in the Programme remains marginal (2% of the submitted projects).

➔ *A Strong Medical Component in the Projects*

The funded projects were mainly in the CSO[3] categories "*Treatment*" (47% of the projects) and "*Early detection, diagnosis and prognosis*" (29% of the projects). The proportion of clinical-oriented projects is higher than within all cancer projects during the same period on the IRCP database[4]. The requirement of the call to have a medical application over the long term in the projects has therefore been well followed.



The category "*Scientific models*" (15% of projects) is also more present in the PMSI Programme than in cancer research in general, in accordance with the scope of the call that includes projects at the interface between mathematics and oncology.

➔ *A Structuring Impact on Research at the Interface of Physics, Mathematics and Oncology*

The multidisciplinary nature of the Programme was an invitation to bring together different partners from different fields and institutions. New collaborations have been created at the national level to answer the call for projects, with consortia having in average 2,8 partners. Almost half of them (44%) were consortia gathering 3 or more disciplines. The remaining consortia were mainly physics-medicine (22%) or physics-biology (19%) consortia.

The Programme has also a structuring impact beyond the projects as it has been instrumental in the creation of strategical axis in research institutions, the creation of new laboratories, as well as new academic and industrial collaborations around the world.

Outcomes of the PMSI Programme*
(51 projects 2011-2013)

Structuring impact in research

- 2 strategical axis at the interface between physics/biology : *Proton Imagery* at IN2P3, *Modelling, physics and mathematics of life* at Idex Université de la Côte d'Azur
- 2 international laboratories: mixed international research unit SMMIL-E (CNRS-Lille University-Tokyo University), associated international laboratory with Taiwan (*Academia Sinica, Institute of Physics*, Taipei)
- 15 academical collaborations in Europe and the rest of the world;
- 10 collaborations with industrial partners in France, Europe and the rest of the world

Lever effect on funding for PIs

- 5 "Investissement d'Avenir"
- 2 european commission (1 FP7, 1 ERC consolidator)
- 2 ANR
- 5 PMSI
- 1 PL-BIO INCa (Cancer Plan)
- 5 Industrial contracts

** as mentioned in the final reports*

[3] The CSO (Common Scientific Outline) is a universal scientific classification system that covers all domains in cancer research.
[4] Data from the IRCP (*International Cancer Research Partnership*) database.

➔ *A Lever Effect on the Projects*

By the end of the funding, an important number of projects (40%) had already secured a new grant, be it a national or European funding or a contract with industrial partners, to continue their project beyond the PMSI programme.

New Tools to Better Understand, Detect, or Treat Cancer

The second objective of the PMSI Programme was to foster the development of new tools for diagnosis or cancer treatment. The ex post analysis on the funded projects between 2011 and 2013 shows that this objective has been reached: the 51 projects allowed the development of more than 60 tools or models, many of which are ultimately for diagnosis or therapeutic purposes.

Tools and models developped in the PMSI Programme* (51 projects 2011-2013)

- Dose calculation modules (11), image processing methods (9) for diagnosis or tissue physical properties assessment, encapsulated nanoparticle (1);
- Experimental setups/methodologies (18) to study cancer cells and the impact of ionisation/nanoparticles on cells;
- Mathematical/theorical models (13) of tumour growth or response to ionisation/nanoparticles;
- Particle detection devices (5), miniaturised imaging devices (2), endomicroscopes (2).

** as mentioned in the final reports*

The Programme has been supporting projects with long-term perspectives as the majority of them (57%) were continuing after the funding. In about the third of the cases, perspectives were characterizations and validations before possible uses in clinical care, and another third was the testing or the development for further uses of the tools or models developed, including beyond oncology (e.g., a tool for assessment of tissue elasticity now also used to study cornea).

The diagnosis and therapeutic component of the programme has led to economical valorisation activities. The 51 projects led to 9 patent requests (4 already accepted at the time of reporting, including one also requesting an international extension), the creation of 2 start-ups and discussions with industrial partners for technological transfer.

Many of the tools generated were already made available to the scientific community, namely simulation modules for medical imagery and radiotherapy on the GATE and GIANT-4DNA platforms in open access, and a experimental radiation device that has been installed on an shared platform.

New Aspects of Cancer Cells Unravelled

The third objective of the Programme was to improve cancer understanding. Even if most of the tools generated were for diagnosis and therapeutic purposes, several of them (mainly

Scientific knowledge generated in the PMSI Programme* (51 projects 2011-2013)

- Characterisation of biophysical properties (stiffness) of cancer cells (3);
- Characterisation of behaviour and effects of nanoparticles on cells (3);
- Modelling of tumour growth, and effects of ionisation;
- Fundamental biology (2): precise subcellular localisation of junction proteins, role of polymerase theta.

** as mentioned in the final reports*

experimental setups, methods, and models) could help to improve the knowledge of biological processes in oncology, but also in fundamental biology.

Publications in the frame of the PMSI programme* (51 projects 2011-2013)

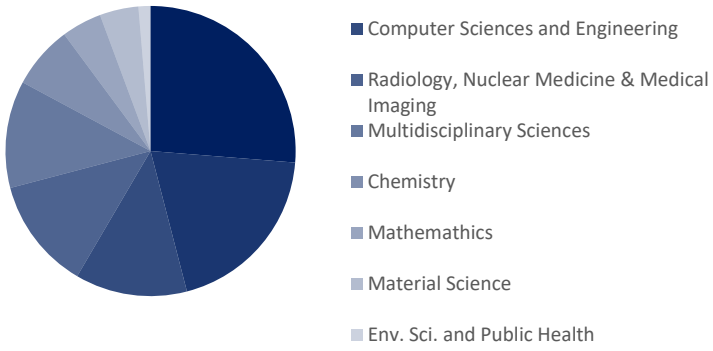
- 121 original articles;
- 15 conference proceedings;
- 8 reviews;
- 4 editorials;
- 2 letters.

** as mentioned in the final reports*

The 51 projects funded between 2011 and 2013 led to at least 150 publications, as mentioned in the final reports. Half of these publication were in open access in accordance to the Cancer Plan objective of "*sharing knowledge and data nationally and internationally between professionals [and the lay public*]."

The multidisciplinary nature of the programme is reflected by the great diversity of the scientific domains covered by the scientific journals in which the 121 articles have been published. Domains related to physics are the most represented (multidisciplinary physics, optics, nuclear science and technology, condensed matter physics, and others) (26% of the publications), followed by biomedical sciences (20%). Nuclear medicine and Computer sciences and engineering (12% each), chemistry (7%), mathematics and material sciences (4% each) and environmental sciences and public (1,5%) were also present. Multidisciplinary journals have published 12% of the articles of the programme.

Original articles: Publication domains of the journals



Conclusion

In 7 editions, the ITMO Cancer-Aviesan PMSI Programme managed to foster a genuine interdisciplinary research ecosystem at the interface between physics, mathematics, engineering sciences and oncology. The Programme also demonstrated its ability to generate new knowledge on the processes in oncogenesis and to generate and disseminate new tools.

The selection committees have noticed an increase of high-quality project submissions over the years, indicating that the scientific community in France related to the Programme's topics got stronger. The quality of the projects is recognized as many PI obtained further funding to pursue them.