aviesan

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

ITMO Cancer

2011.

A DECADE OF INVOLVEMENT
IN CANCER CONTROL PLANS

.2021

contents

editorial.

The Multi-Organisation Thematic Institute (ITMO) Cancer, part of the Aviesan Alliance, has worked towards for over a decade to develop and support cancer research in France. Alongside the National Cancer Institute (INCa), it has contributed to the development of the national Cancer Control Plans 2 & 3, and now the 2021-2030 Ten-year Cancer Control Strategy.

One of the main objectives of the ITMO is to open up the field of oncology to other disciplines beyond the realms of cancer biology. It is under these conditions that the calls for proposals in mathematics, computer science, chemistry, physics and engineering sciences have led to the funding of dozens of projects driven by experts in these fields. They have opened up new and unexpected research avenues, thereby reinforcing the key role of interdisciplinarity in oncology.

Similarly, it is the ITMO's priority to promote research in emerging themes in order to allow their appropriation and sufficient maturation to access recurrent funding from national agencies such as INCa, or even internationally.

For example, we can cite the call for proposals that has led to better structuring of the French scientific community around the theme of tumour heterogeneity, as well as those dedicated to epigenetics and alternative models. They have also opened up oncology to teams that do not use their talents in this field, making a very significant contribution to reinforcing research potential within it.

To complement this, the ITMO has set up a recurring call for proposals dedicated to equipment, aimed at reinforcing the state-of-the-art technological platforms that are now essential for a better understanding of the complexity and heterogeneity of cancer in all its dimensions.

Furthermore, mindful of the importance of the basic-translational-clinical research continuum, the ITMO has encouraged research training for young doctors, pharmacists and veterinarians through the funding of Research Masters (2nd year), PhDs and post-doctorates. The success of this programme is thereby illustrated by over one hundred PhDs funded over the past 10 years.

Finally, it must be noted that the ITMO is implementing a number of actions by building long-term partnerships: for example, with the CNRS and Inserm Atip-Avenir programme, to promote the emergence of new oncology teams, or with Anses, to support research into the environmental causes of cancer.

New scientific and technological challenges are continually emerging in the field of oncology. Hence, ITMO's experts regularly contribute to their formulation in order to enable their effective consideration.

The decade 2011-2021 has provided sufficient hindsight to highlight lessons that shed light on the success of most of the actions carried out by the ITMO. Their synthetic presentation in this document will enable readers to understand the extent of the driving force and federating role of the Aviesan ITMO Cancer in the French research community, which is its *raison d'être* and source of pride within the Alliance ●

Alain Eychène and Yvan de Launoit
Directors of the Aviesan Cancer ITMO

Muriel Altabef
Assistant Director of the Aviesan Cancer ITMO

00.

AVIESAN, TO INCREASE THE PERFORMANCE OF FRENCH RESEARCH IN LIFE SCIENCES AND HEALTH

Essential coordination

A complex research landscape

In 2008, main institutions shared the observation that numerous entities – operators or funding agencies – were involved in life sciences and health research in France. While they were all justified, they were not part of a real national coordination in which their role and scope were precisely determined.

This lack of coordination had long been a handicap in several ways:

- for laboratories, particularly in terms of management and of search for additional funding;
- for the capacity of public research to develop vast research programmes and partnerships with industry, and therefore support a high level of value creation from technology and innovation;
- for the deployment of sufficient resources when new approaches or research methods emerge, or in the face of a health crisis;
- and for the international visibility of the French research system, and its ability to establish structural partnerships.

AVIESAN: 6 FOUNDING OBJECTIVES TO DYNAMISE FRENCH RESEARCH IN LIFE SCIENCES AND HEALTH

1. **Develop, at the highest level in all research fields** in the life sciences and health, a continuum ranging from basic research to the applications of that research.

2. **Strengthen partnerships between universities and research bodies,** ensuring the national coherence of the projects [...], particularly in terms of themes and infrastructure.

3. **Ensure knowledge dissemination and value creation** from research, whether industrial, clinical or social.

4. **Ensure the consistency of the actions and methods** of support [*of the signatories of the agreement, ed.]* for the research.

5. **Define common positions,** particularly in terms of European research and international cooperation, according to existing or future partnerships.

6. **Harmonise and simplify administrative procedures** for the laboratories.

Federate in order to simplify

To overcome these obstacles, a solution has taken hold: form an alliance of the major research operators. Aviesan, the French National Alliance for Life Sciences and Health, brings together the country's 9 principal research operators in the field: CEA, CNRS, France Universités, Inrae, Inria, Inserm, Institut Pasteur, IRD and Réseau CHU[(1)]. It also hosts, as associate members, 11 research institutes, establishments or federations of establishments operating in the biomedical field, which participate in a certain number of its projects.

The members of Aviesan collectively defined the objectives of their coordination, which are laid down in the founding agreement of the Alliance signed on 8 April 2009.

The Aviesan ITMOs, multi-organisation functional bodies

Aviesan is organised into 9 Multi-Organisation Thematic Institutes (ITMOs) covering all major fields in the life sciences and health. Each ITMO has a multidisciplinary committee of experts from the various founding bodies of Aviesan.

The ITMOs are jointly managed, most of which by CNRS/Inserm, with the CEA and Inrae involved in the joint management of one ITMO each.

THE AVIESAN ITMOS: 9 KEY AREAS FOR COVERING RESEARCH IN LIFE SCIENCES AND HEALTH

1. Molecular and structural basis of life sciences
2. Cell biology, development and evolution
3. Cancer
4. Genetics, genomics and bioinformatics
5. Immunology, inflammation, infectiology and microbiology
6. Neurosciences, cognitive sciences, neurology and psychiatry
7. Physiopathology, metabolism and nutrition
8. Public health
9. Health technologies

(1) CEA (French Alternative Energies and Atomic Energy Commission), CNRS (French National Centre for Scientific Research), France Universités (Assembly of Executive directors of French universities, National polytechnic institutes, Écoles normales supérieures, Grandes écoles, and Research and higher education clusters), Inrae (French National Research Institute for Agriculture, Food and Environment), Inria (French National Institute for Research in Digital Science and Technology), Inserm (French National Institute of Health and Medical Research), IRD (French National Research Institute for Sustainable Development), Réseau CHU (Assembly of Managing directors of French university hospitals).

Strategic orientations

In 2010, for the first time at national level, an exhaustive assessment of the activities, competences and resources at hand for each of the major research fields was carried out by the ITMOs. They also analysed the strengths and weaknesses and identified priority areas for research. Brought together within strategic orientations for each major research domain, these assessments provided the Aviesan Board with a valuable basis for reflection, concerning:

- the operational coordination of the various operators, particularly major research bodies and universities;
- the consultation on scientific policy issues in the field of the life sciences and health, particularly with the supervisory authorities.

This operation was repeated in 2013 when preparing the Alliance's contribution to the National Research Strategy. The Aviesan ITMOs therefore play an essential scientific coordination role, providing France with enhanced strategic analysis capacities in the field of the life sciences and health.

Facilitation of scientific communities

In parallel, the ITMOs carry out actions aimed at supporting reflection within their entire community, all operators combined, promoting interdisciplinary dialogue, and showcasing research nationally – including with regard to industry and patient associations – and internationally, particularly through the organisation of meetings and colloquia.

The ITMOs can also play a direct role in the programming of research at national level, either occasionally or recurrently: this is particularly the case of the Aviesan ITMO Cancer •

THE AVIESAN ITMOS: 2 MAJOR COORDINATION MISSIONS

1. **Develop strategic orientations** in their scientific field, based on their multi-organisation and multidisciplinary expert committee.

2. **Develop concrete facilitation actions** to improve the competitiveness of their community and showcase it internationally.

01.

ITMO CANCER, A SINGULAR POSITIONING FOR A PRIORITY ISSUE

A specific context: the National Cancer Control Plans

France's project to fight cancer began on the initiative of the Head of State in 2002, at a time when the disease was the leading cause of premature mortality in the country. Within the space of 20 years, three Cancer Control Plans, driven at the highest level, have been designed and implemented, and a Ten-year Cancer Control Strategy is now operational for the 2021-2030 period.

The Cancer Control Plans have always favoured an integrated approach to fighting the disease, covering prevention, organisation of care and support for research, simultaneously. This global strategy has particularly been adopted to promote the decompartmentalisation of the players involved in fighting cancer: thanks to the cross-cutting nature of the recommended actions, synergies have emerged, for the benefit of a better management and understanding of the disease.

RESEARCH IN THE NATIONAL CANCER CONTROL PLANS

2003-2007 1ST CANCER CONTROL PLAN

Dynamise and better coordinate cancer research. Drive it to the highest international level of excellence.
Measures 66 to 70

- **Form (inter-)regional cancer hubs *('Cancéropôles')*, ensuring a research-to-care continuum, combining hospitals of reference and accredited research units.**
- **Found the National Cancer Institute – Adopt a programme-driven research policy that promotes partnerships between public and private research.**
- **Support the emergence of international sites – Develop international cooperation, particularly within the framework of Europe.**

2009-2013 2ND CANCER CONTROL PLAN

Ensure the rapid transfer of research advances for the benefit of all patients.
Measures 1 to 5

- **Reinforce multidisciplinary research resources.**
- **Understand and reduce cancer inequalities through research.**
- **Characterise environmental and behavioural risks.**
- **Dynamise clinical research.**
- **Make France an international reference.**

2014-2019 3RD CANCER CONTROL PLAN

Cure more patients.
Objectives 1 to 9

- **Accelerate the emergence of innovation for the benefit of patients.** *(Objective 5)*
- **Reinforce French progress in personalised medicine.** *(Objective 6)*
- **Reduce the impact of cancer on personal life.** *(Objective 9)*

Invest in prevention and research.
Objectives 10 to 13

- **Prevent occupational and environmental cancers.** *(Objective 12)*
- **Provide the means for innovative research.** *(Objective 13)*

Optimise steering and organisation.
Objectives 14 to 17

- **Optimise organisation for greater efficiency.** *(Objective 16)*
- **Adapt funding methods to the challenges of oncology.** *(Objective 17)*

Unity of leadership for cancer research

Coordination is an essential aspect of the national cancer control plans. The 1st Cancer Control Plan recommended the creation of the National Cancer Institute (INCa), which was inaugurated in 2004. As an agency for health and scientific expertise placed under the supervision of the Ministry of Solidarity and Health and the Ministry of Higher Education, Research and Innovation, INCa is tasked with coordinating actions to fight cancer on a national level.

The 2nd Cancer Control Plan recommended in its measure no. 5 to *'clarify the organisation and interactions between the agencies, research organisations and INCa, define how they are linked and establish rules to stabilise them over the long term, by maintaining unity of leadership for cancer research'*. The formalisation of the link between INCa and the Aviesan ITMO Cancer became effective in 2011: the director of INCa's Research and Innovation division is also one of the directors of the ITMO.

The 3rd Cancer Control Plan, in action 16.1 of its component on steering the fight against cancer, perpetuated this link, recommending to *'guarantee the unity of duties of the Research Director of INCa and the Director of the Aviesan ITMO Cancer'*.

The particularity of programming thematic research

Like the other ITMOs, the ITMO Cancer is in charge of coordinating basic research within its theme, through the formulation of strategic orientations and the development of facilitation actions intended for its community.

However, the successive Cancer Control Plans have had a direct impact by amplifying and expanding the missions of the ITMO. This is the case of its first mission relating to the strategic orientations, with these having contributed majorly to the design of the research component of the Cancer Control Plans.

These same strategic orientations are also concretely implemented by the ITMO in its own research programmes, funded outside of the ANR on Cancer Control Plan credits managed by Inserm. Such a mission to program themed basic research gives the ITMO a singular position within the Alliance.

This programming and funding activity began in 2011 within the framework of the 2nd Cancer Control Plan. During that year, INCa and the ITMO jointly programmed 2 calls for thematic research proposals and 1 call for research training applications.

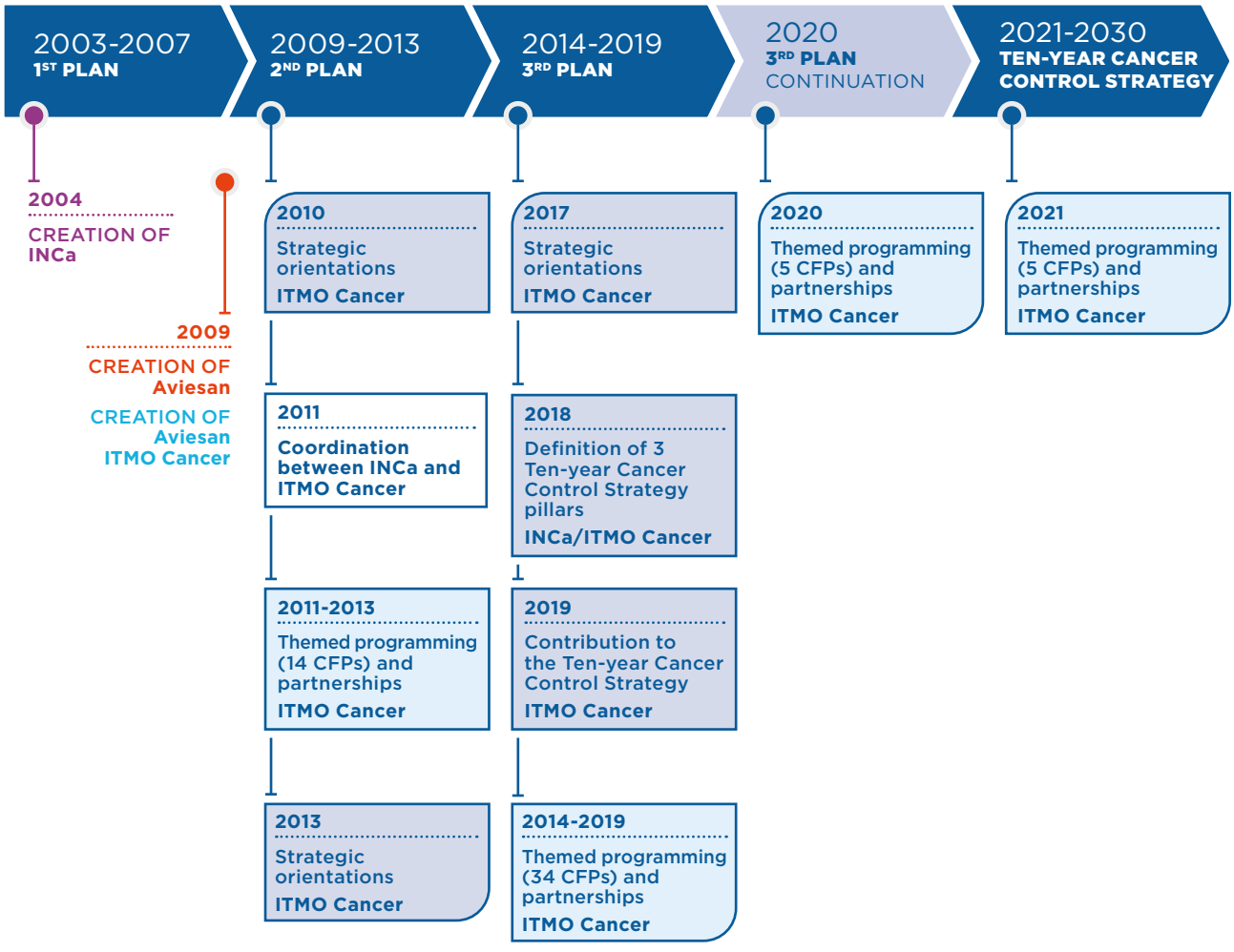
AVIESAN ITMO CANCER: 3 MISSIONS SERVING FRENCH RESEARCH IN ONCOLOGY

1. **Formulate major strategic orientations** for cancer research.
2. **Implement the strategic orientations into themed research** partnerships and programmes funded by the Cancer Control Plans.
3. **Animate the French research community** in oncology and showcase it internationally.

The ITMO then fully took on the mission of programming themed basic research, reinforced by its nomination as being (jointly) responsible for 17 actions of the 3rd Cancer Control Plan, especially and mainly action 13.1: *'Guarantee the independence and creativity of the research by ensuring a funding rate for oncology basic research that exceeds 50% of the credits of all the calls for proposals by INCa and Aviesan cancer'*.

Over the past 20 years, the national cancer control strategy adopted by France has therefore led to the Aviesan ITMO Cancer being involved both in devising the Research components of the Cancer Control Plans and Ten-year Cancer Control Strategy through the definition of major strategic orientations, and in implementing them through its programming, partnership, funding and facilitation actions •

DEVISING AND IMPLEMENTING THE CANCER CONTROL PLANS: INVOLVEMENT OF THE AVIESAN ITMO CANCER (2011/2021)



02.

ITMO CANCER, A DECISIVE ROLE IN THE CANCER RESEARCH STRATEGY

Supported by a multidisciplinary Expert Committee

The Aviesan ITMO Cancer senior management seeks advices from a selection of experts gathered in a Committee that reflects the multidisciplinary nature of the cancer theme and the diversity of the Alliance. Since 2011, the Committee has seen a succession of scientists from the various fields of oncology, and also specialists in mathematics, physics, chemistry and computer science involved in cancer research, as well as clinicians. All of the major research bodies (CEA, CNRS, Inrae, Inria, Inserm, Institut Pasteur), as well as the university and hospital spheres, are represented on the Committee.

The 15-20 member committee is regularly renewed and meets thrice yearly to be informed of the actions undertaken by the ITMO within the framework of its roadmap, and to reflect on points on which senior management wishes to obtain its opinion. It has also been convened in extraordinary sessions several times since the creation of the ITMO, during seminars dedicated to the definition of strategic orientations for the design of the Cancer Control Plans and the Ten-year Cancer Control Strategy, or to develop, in the meantime, recommendations for research activities.

The strategic orientations, cornerstone of the research policy

The definition of strategic orientations for research is one of the core missions of the ITMOs. In 2010, following the founding of Aviesan, an initial exercise was carried out for all of the themes, to support reflection by the Alliance Board.

In 2013, the ITMO Cancer experts repeated the operation, together with the members of the INCa Scientific Advisory Board, within the framework of the Alliance's contribution to the National research strategy and in preparation of the 3rd Cancer Control Plan. These strategic orientations for 2013 were centred around: the identification of major challenges covering the entire cancer problem; an overview of the cancer research landscape in France; recommendations on priority research areas and recommendations concerning the organisation of the research.

2013 STRATEGIC ORIENTATIONS: CHALLENGES TO CONSIDER AND AREAS TO PRIORITISE IN THE 3RD CANCER CONTROL PLAN

CHALLENGES

- Scientific:
  - > redefine tumour diseases by studying the physiological mechanisms of the cell and its interactions with its environment, in order to understand pathological deregulations.
- Medical and public health:
  - > research and innovation, to move from precision medicine to personalised medicine;
  - > primary prevention research, particularly on risk behaviours and on the analysis and correction of its failures;
  - > research to identify populations exposed to the risk of cancer and facilitate their follow-up with early-diagnosis strategies (secondary prevention).

RESEARCH AREAS

- Genomics and personalised medicine
- Medicines, molecular pharmacology and biomarkers
- Metabolism, infection, inflammation, immunology and cancer
- Epidemiology, epigenetics and environment
- Human and social sciences and public health
- Systems biology
- Physics-mathematics and cancer interfaces
- Clinical research
- Training and value creation

In 2017, the ITMO once again set about defining strategic orientations, with two primary objectives: constitute the scientific basis for its programming and anticipate the future Ten-year strategy for the fight against cancer.

These strategic orientations stem from the reflection by thematic groups that were formed within the Expert Committee in 2016. Their work was presented and discussed in a plenary meeting at the beginning of 2017. From these elements of reflection, a framework emerged that was centred around 3 areas and 30 objectives, subsequently clarified by the Committee and finalised by ITMO Cancer senior management. The document *Orientations stratégiques 2017 (2017 Key Strategic Trends)* was communicated to INCa and to the supervisory ministries of the research bodies, and then published on the ITMO website. These orientations have contributed to the development of research recommendations for the future 2021-2030 Ten-year Cancer Control Strategy coordinated by INCa.

Two steps followed, the first (2018) involving a joint seminar with the INCa Research and Innovation division, which led to the definition of three priority challenges. The second (2019) again focused on the mobilisation of ITMO experts. The Committee was therefore called upon to roll out the most relevant basic-research avenues for addressing each of these challenges. These research recommendations were summarised in the document *Contribution de l'ITMO Cancer d'Aviesan à la Stratégie décennale* communicated to INCa and published.

In 2019, an extract from the *Orientations stratégiques 2017* document concerning the theme of mathematical aspects and data was produced and distributed, in order to feed the community's reflection on the new mathematical approaches to modelling, mining, statistical learning and big data analysis, a research field that is currently expanding, particularly in oncology.

In September 2021, the INCa Research and Innovation division and the ITMO Cancer (senior management and Expert Committee) met for a working seminar. The objective was to identify avenues for reflection to supplement or update the previous research recommendations issued in the 2017 Key Strategic Trends and the 2019 Contribution, as well as the elements of the 2021-2025 roadmap for the Ten-year Cancer Control Strategy. These new recommendations for action, which are being argued and drafted in 2022, will be called upon to feed into the reflection on the 2026-2030 component of the Ten-Year Cancer Control Strategy ●

CONTRIBUTION OF THE AVIESAN ITMO CANCER TO THE 2021-2030 TEN-YEAR CANCER CONTROL STRATEGY: A 3-STEP APPROACH, INITIATED IN 2017

1. Aviesan ITMO Cancer

> Expert Committee seminar (February 2017)

2017 Key Strategic Trends

2. INCa/Aviesan ITMO Cancer

> Seminar for joint reflection by the INCa Research and Innovation division and the ITMO senior management (June 2018)

3 pillars of the Ten-year Cancer Control Strategy

> Participation of the ITMO senior management on the INCa French and international Scientific Advisory Boards

3. Aviesan ITMO Cancer

> Expert Committee retreat (February 2019)

Contribution to the 2021-2030 Ten-year Cancer Control Strategy

4. INCa/Aviesan ITMO Cancer

> Seminar for joint reflection by the INCa Research and Innovation division and the ITMO Expert Committee and senior management (September 2021)

Reflection on the 2026-2030 component of the Ten-year Cancer Control Strategy

RESEARCH RECOMMENDATIONS TO INSPIRE THE TEN-YEAR STRATEGY

KEY STRATEGIC TRENDS (2017, EXTRACTS)	3 PILLARS OF THE TEN-YEAR CANCER CONTROL STRATEGY (2018)	CONTRIBUTION TO THE TEN-YEAR CANCER CONTROL STRATEGY (2019, EXTRACTS)
• Study cancer through its evolution, particularly the early, pre-neoplastic and potentially reversible stages. • Continue to elucidate the mechanisms of cancer, the adaptive dynamic of tumours, genetic and non-genetic plasticity. • Study the role of the non-coding genome in tumorigenesis. • Continue to identify risk factors: genetics, environment, nutrition.	Prevent the emergence of the disease	**FUNDAMENTAL MECHANISMS OF ONCOGENESIS AT DIFFERENT SPATIAL AND TEMPORAL LEVELS** • Move forward in the comparative description of the biology of the normal cell and the cancer cell. • Study the mechanisms of transition from healthy to cancerous cell. • Study the impact of ageing on the healthy cell. **CANCER RISK FACTORS AT CELL AND POPULATION LEVEL** • Decipher the mechanisms of action of the risk factors. • Study multiple-risk situations. • Better control risk and its consequences.
• Understand dormancy and the mechanisms of resistance. • Facilitate drug design and the repositioning of older agents. • Identify the biomarkers predictive of a successful therapeutic approach. • Promote the new biomarkers for early diagnosis and monitoring (treatment toxicity, prediction of relapse and resistance). • Develop methods to stratify responders and predict clinical benefit.	Prevent relapse	**TREATMENT RESISTANCE** • Analyse the molecular and cellular mechanisms of resistance. • Elucidate the role of intratumoural heterogeneity in resistance. **POST-TREATMENT LONGITUDINAL FOLLOW-UP** • Determine the components of residual-disease monitoring and identify the markers of relapse. • Model longitudinal monitoring to predict relapse. • Evaluate the role of behavioural or environmental factors and comorbidities in the risk of relapse.
• Place the person with cancer as an actor at the centre of research. • Refine pre-clinical models to validate therapies and understand the side effects of therapies.	Prevent sequelae, toxicity and side effects	**TOXICITY AND SIDE EFFECTS OF TREATMENTS** • Reinforce toxicity studies. • Identify biomarkers predictive of drug toxicity. • Evaluate the impact of interindividual variability on toxicity. **TREATMENT-RELATED SEQUELAE** • Improve the delivery of treatments (vectorisation, etc.). • Adjust the dose (therapeutic de-escalation). • Identify treatment combinations to reduce doses. • Evaluate the role of post-treatment behaviours and environment on sequelae and side effects.

03.

ITMO CANCER, A LEADING ROLE IN BASIC RESEARCH PROGRAMMING

Close to 60 calls for proposals by the Aviesan ITMO Cancer

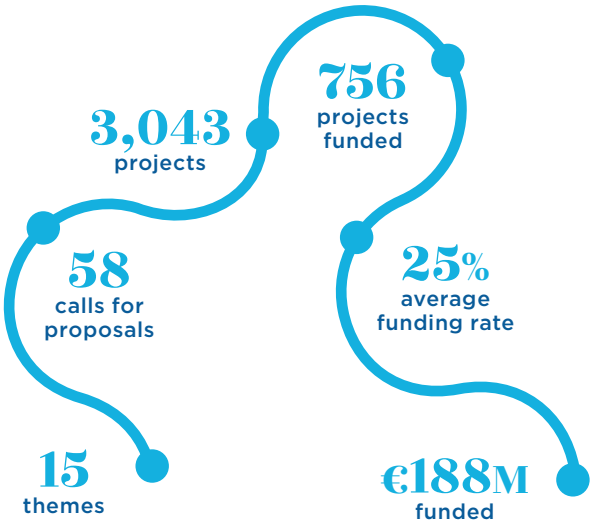
Since 2011 and the first calls for proposals launched in conjunction with INCa, the Aviesan ITMO Cancer has developed a sustained programming activity through the launch of several calls for proposals each year. The detailed data from this programming (programme objectives, scientific content of the projects funded, amounts allocated) are the subject of an exhaustive account each year in the INCa annual scientific report *Actions for cancer research* (see for example the 2020 scientific report).

During the 2011-2021 period, the ITMO calls for proposals were funded by Cancer Control Plan, Cancer 2020 and Ten-year Cancer Control Strategy credits administered by Inserm.

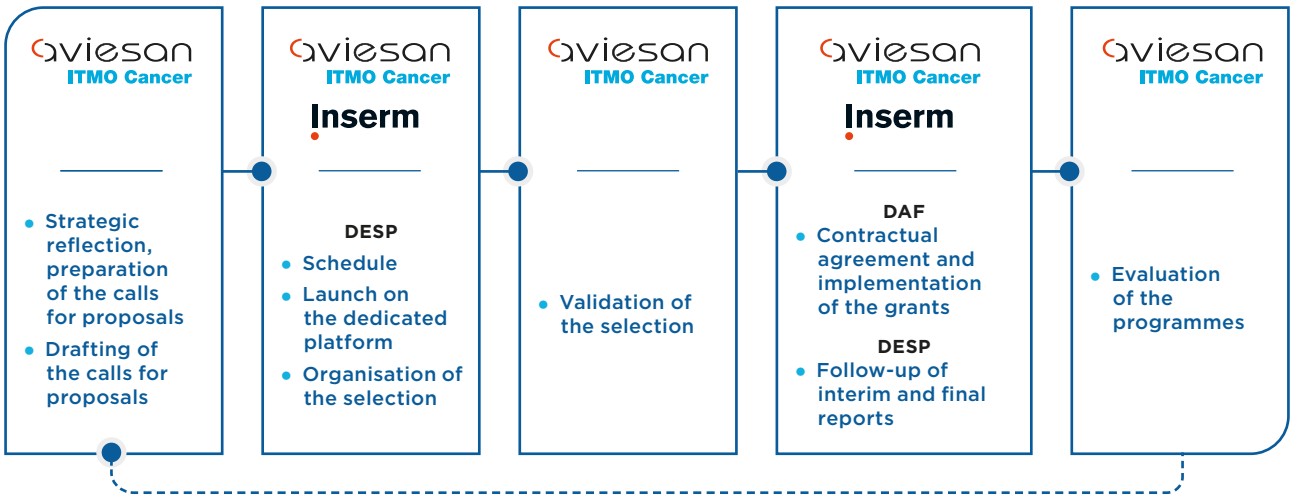
In close collaboration with the ITMO, Inserm also ensured, *via* its departments Programme Assessment and Follow-up (DESP) and Financial Affairs (DAF), a large part of the operational management of the calls for proposals: constitution of selection committees, organisation of project selection, contractual agreement and monitoring.

Between 2011 and 2021, the ITMO supported 756 projects for an overall budget of close to €188 million. The selection rates per programme ranged from 8% to 31% over the period, and 25% for all programmes taken together, i.e. 5 points off the long-term objective set by the *Loi de programmation de la recherche* (Research Programming Act) promulgated in 2020.

THE 2011-2021 PROGRAMMING IN FIGURES



CALLS FOR PROPOSALS MANAGED IN COLLABORATION WITH INSERM



2011-2021 PROGRAMMING: 15 THEMES ADDRESSED

PROGRAMME	OBJECTIVES	COMMUNITIES OR DISCIPLINES TARGETED
FRFT(-DOC)	Promote the training and professional development of young graduates in medicine, pharmacy, odontology and veterinary medicine by funding Master's degrees, PhDs and post-doctorates in oncology (-doctorates only from 2021).	Medicine, pharmacy, veterinary medicine
EQUIPMENT	Assist in the acquisition of shared semi-heavy or heavy equipment, to enable laboratories to conduct ambitious and innovative cancer research, while promoting interactions between teams and strengthening the attractiveness and position of French teams on the international scene.	Oncology basic research community
PMSI	Increase the interest of physics, mathematics and engineering science researchers (PMSI) in cancer research, to improve the understanding, diagnosis and treatment of cancer.	Physics, mathematics, engineering sciences
PCSI	Improve the understanding of cancer and its prognosis through concepts or tools derived from physics, chemistry and engineering sciences (PCSI).	Physics, medical physics, biophysics, chemistry, bio-chemistry, engineering sciences
MIC	Improve the understanding of cancer and its prognosis through mathematics and computer science (MIC).	Mathematics, statistics, computer science
SPONTANEOUS TUMOURS	Promote the integration of studies on spontaneous cancers in animals in the overall study of cancer in humans.	Oncology basic research community, veterinary medicine
CANCER AND ENVIRONMENT	Develop tools evaluating the impact of environmental factors on the development of cancer. Understand the mechanisms underlying the development of cancer following exposure to environmental factors.	Oncology basic research community, clinical, toxicology, mathematics
SYSTEMS BIOLOGY	Support the development of multi-scale data integration models (molecule, cell, tissue, organism, clinical) in the field of cancer.	Oncology basic research community, clinical, mathematics, physics, chemistry, computer science
EPIGENETICS AND CANCER	Characterise the epigenetic mechanisms at work within cancer cells and in their microenvironment, particularly through the use of high-quality epigenome reference maps.	Oncology basic research community, bioinformatics
SINGLE CELL	Promote research based on a single cell approach, in order to identify or characterise the factors involved in the emergence or progression of tumours.	Oncology basic research community
NON-CODING RNAs	Promote the identification of non-coding RNAs and the study of their mechanisms of action, regulation and involvement in oncogenesis.	Oncology basic research community
3Rs	Support the implementation of the principles of the 3Rs (Replacement, Reduction and Refinement) in the oncology research field.	Oncology basic research community
PRE-NEOPLASIA	Promote the multi-scale spatial and temporal characterisation of lesions with malignant potential, in order to identify intervention targets and stratify lesions according to their risk of progression.	Oncology basic research community, clinical
TUMOUR HETEROGENEITY AND ECOSYSTEM (HTE)	Constitute a critical mass of resources and skills to conduct interdisciplinary research on the tumour microenvironment, as part of an integrated vision using mathematical modelling and *in silico* methods.	Cell biology, (epi)genomics, mechanobiology, physics, systems biology, clinical, chemistry, mathematics, computer science
'SUBCELLULAR MAPPING' AVIESAN FEDERATIVE PROGRAMME (PFA)	Pool the know-how and skills of the Aviesan 'Cancer' and 'Molecular and structural basis of life sciences' communities in order to progress towards the structural and functional mapping of the cancer cell.	Oncology basic research community, structural biology, biophysics, biochemistry

Interdisciplinary and themed programming

Interdisciplinarity is one essential aspect of the ITMO's programming. Through its multi-organisational nature, the ITMO fulfils the clearly identified and explicit need in the Cancer Control Plans to open up research to disciplines outside the life sciences and health field. The 2nd Cancer Control Plan recommended prioritising *'the importance of interactions between disciplinary fields'* (measure 1), while the 3rd Cancer Control Plan recommended *'promoting interdisciplinary dynamics within calls for proposals'* (action 13.1). In fact, when faced with the complexity of cancer, as with any complex question, the diversification of approaches and their integration within the same project represent a major asset for the emergence of new promising avenues of knowledge. It is with this in mind that the ITMO has joined forces with other Aviesan ITMOs to programme several of its calls for proposals.

Theming represent a second essential aspect of the ITMO's programming, which supplements INCa's actions in the programming of translational and clinical research, and its free basic research programme. The implementation of targeted programmes stemming from a research strategy coordinated at national level has been a goal since the 1st Cancer Control Plan, in order to *'give a strong impetus to cancer research'*.

2011-2021 PROGRAMMING: OVER 5 CFPs ON AVERAGE EACH YEAR

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	CFPs	PROJECTS	BUDGET (M€)	SELECTION RATE
FRFT	■	■	■	■	■	■	■	■	■	■		10	243	19.56	31%
FRFT-Doc											■	1	8	1.02	22%
Equipment						■	■	■	■		■	5	105	17.16	31%
PMSI	■	■	■	■	■	■	■	■				8	121	35.36	23%
PCSI									■	■	■	3	65	18.58	21%
MIC									■	■	■	3	22	9.7	21%
SpontTum	■	■	■	■								4	10	3.44	33%
K-Env		■	■	■	■	■	■					6	43	18.16	27%
BioSys		■	■	■	■		■					5	26	14.28	18%
EpiK			■	■	■	■						3	34	13.65	30%
Single Cell								■	■	■		2	13	6.12	15%
ncRNAs								■	■	■		2	16	6.65	19%
3Rs									■	■		2	16	6.8	17%
Pre-neoplasia									■	■	■	2	15	8.39	27%
HTE						■	■					1	6	7.56	8%
PFA									■	■		1	13	1.36	21%
												58	756	187.79	25%

FRFT(-Doc): Training in basic and translational research (-doctorates); PM(C)SI: Physics, mathematics (chemistry) and engineering sciences applied to cancer; MIC: Mathematics and computer science applied to cancer; SpontTum: Spontaneous tumours; K-Env: Cancer and environment; BioSys: Systems biology; EpiK: Epigenetics and cancer; ncRNAs: non-coding RNAs; 3Rs: principles of the 3Rs (Replacement, Reduction and Refinement) in oncology; HTE: Tumour heterogeneity and ecosystem; PFA: 'Subcellular mapping' Aviesan federative programme.

This strategy-programming dyad forms the very foundation of the ITMO's activity: the majority of the programmes that it defines and supports constitutes an operational roll-out of its Key Strategic Trends, with the support of *ad hoc* working groups.

Several elements characterised its programming between 2011 and 2021:

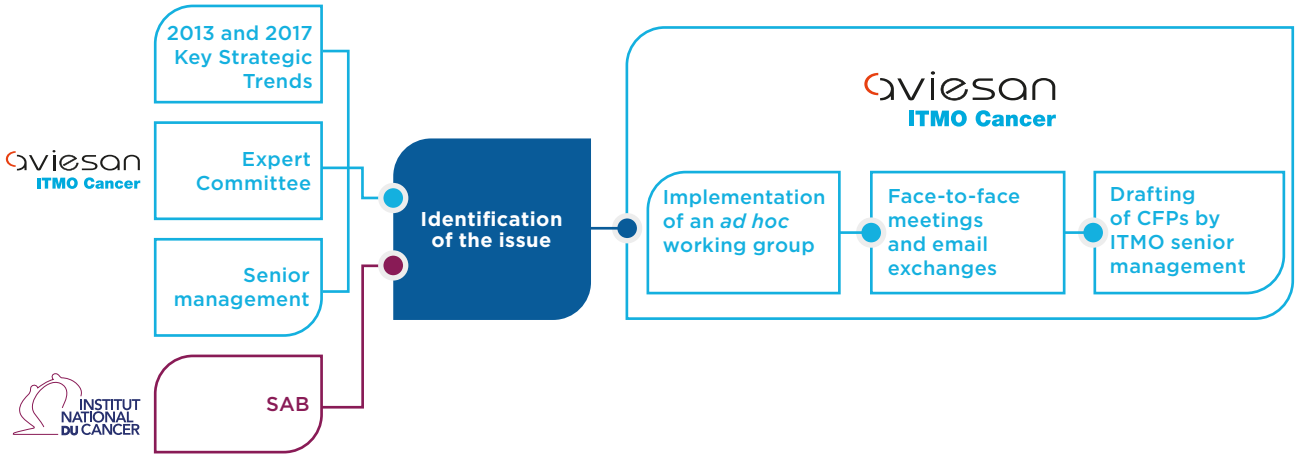
- among the programmed calls for proposals, the vast majority were scientific in nature and 2 were research support programmes (support for training in and through research; help with the acquisition of heavy or semi-heavy equipment);
- some programmes inspired by the strategic orientations were supported over a short period or on a very occasional basis: the main objective was to give a strong impetus to research in an emerging thematic field identified as promising by the ITMO;
- conversely, other programmes were sustained due to their long-term structuring role in research. This is typically the case of the two research support programmes, as well as PMSI and its offshoots PCSI and MIC, stemming from its split in 2019: their aim is to structure an interdisciplinary research ecosystem on cancer over the long term;
- finally, the HTE and PFA-Subcellular mapping programmes were distinguished by their innovative nature, in terms of their format and objectives.

Innovative formats

In 2016 and 2019, the ITMO launched two programmes incorporating new concepts: a step for the co-construction of project(s) by the successful applicants to the themed calls for expression of interest brought together in a consortium, and a component dedicated to the animation of these consortia. The aim of these programmes was to structure and support new communities of scientists around topics considered to be priorities.

The HTE (Tumour Heterogeneity and Ecosystem) and PFA (Aviesan federative programme: Towards a new subcellular map of the cancer cell) shared the same ambition: namely to offer the conditions necessary for the emergence of national interdisciplinary consortia, of sufficient critical mass to make them competitive in both European and international calls for proposals, and enable them to address the challenges of research conducted on particularly complex themes.

THEMES DIRECTLY STEMMING FROM THE STRATEGIC ORIENTATIONS

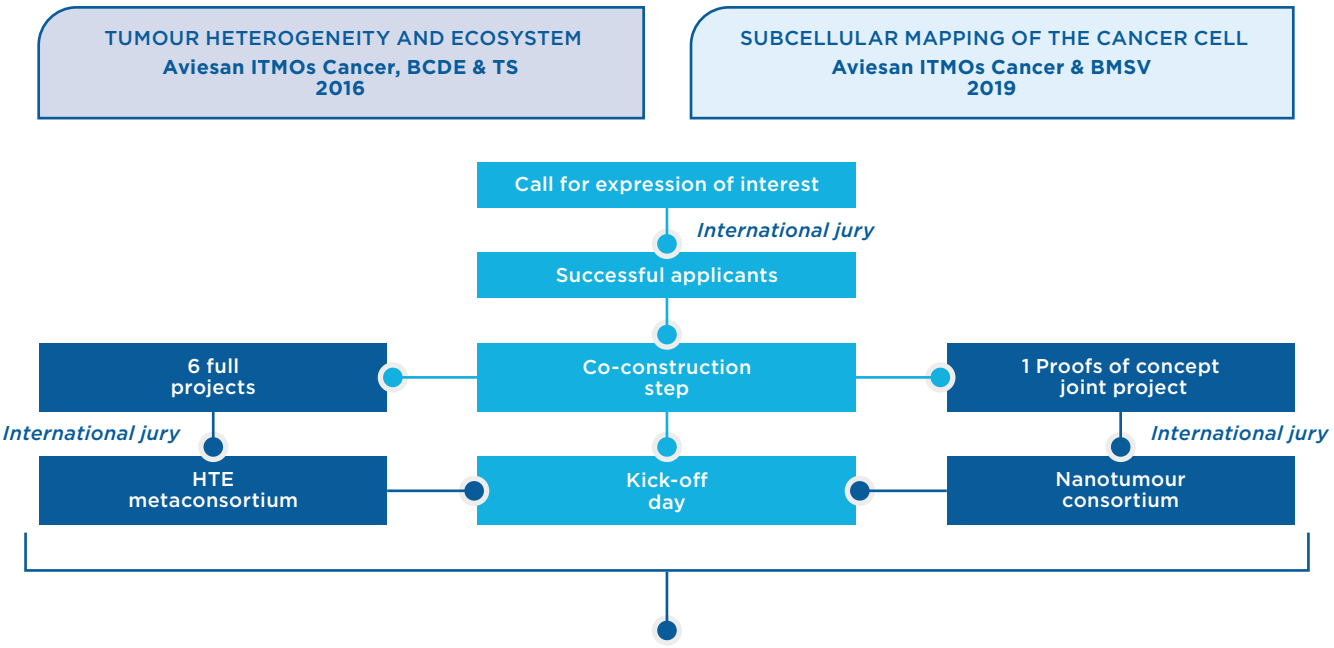


Given the need to address the two targeted themes in an interdisciplinary way, these new programming formats have greatly benefited from the multi-organisation nature of Aviesan. They were developed through close collaboration of the ITMO Cancer with other ITMOs of the Alliance, namely Cell biology, development and evolution (BCDE) and Health technologies (TS) for the first, Molecular and structural basis of life sciences (BMSV) for the second.

Since their launch, these two programmes have been closely monitored by an *ad hoc* scientific committee, which audits the progress made and issues recommendations to the consortium leaders regarding the continuation of the programmes.

The ITMO also held a virtual retreat for the members of the HTE consortium and their teams in March 2021. During this meeting, each of the managers of the 6 research programmes gave an update. A plenary discussion built up around the prospects of the consortium and, more broadly, of tumour heterogeneity research.

CO-CONSTRUCTING NEW INTERDISCIPLINARY COMMUNITIES



HTE METACONSORTIUM: FIGURES AND MISSIONS

- **6 consortia, 39 teams selected.**
- **4 years of funding (€7.6M), 4 areas:**
  - > multidisciplinary research: 6 full projects,
  - > sharing of knowledge and know-how,
  - > sharing of resources,
  - > facilitation of the metaconsortium (training, communication).

NANOTUMOUR CONSORTIUM: FIGURES AND MISSIONS

- **1 consortium, 13 teams selected.**
- **3 years of funding (€1.4M), 2 areas:**
  - > multidisciplinary research: 1 Proofs of concept joint project,
  - > facilitation of the consortium.

BCDE: Cell biology, development and evolution; BMSV: Molecular and structural basis of life sciences; TS: Health technologies.

The added value of programme evaluation

In order to *'Maintain a high level of requirement in the choices of research funding'*, the 3rd Cancer Control Plan recommended in its actions 17.12 and 17.13 to *'Reinforce the scientific monitoring of the projects funded'* and *'Develop shared tools for evaluating cancer research projects'*. In line with this, the INCa International Scientific Advisory Board requested the organisation, at national level and bringing all funding providers together, of reflection on the evaluation of the research programmes supported within the framework of the Cancer Control Plans: the Aviesan ITMO Cancer has participated in the *ad hoc* working group set up by INCa since 2017.

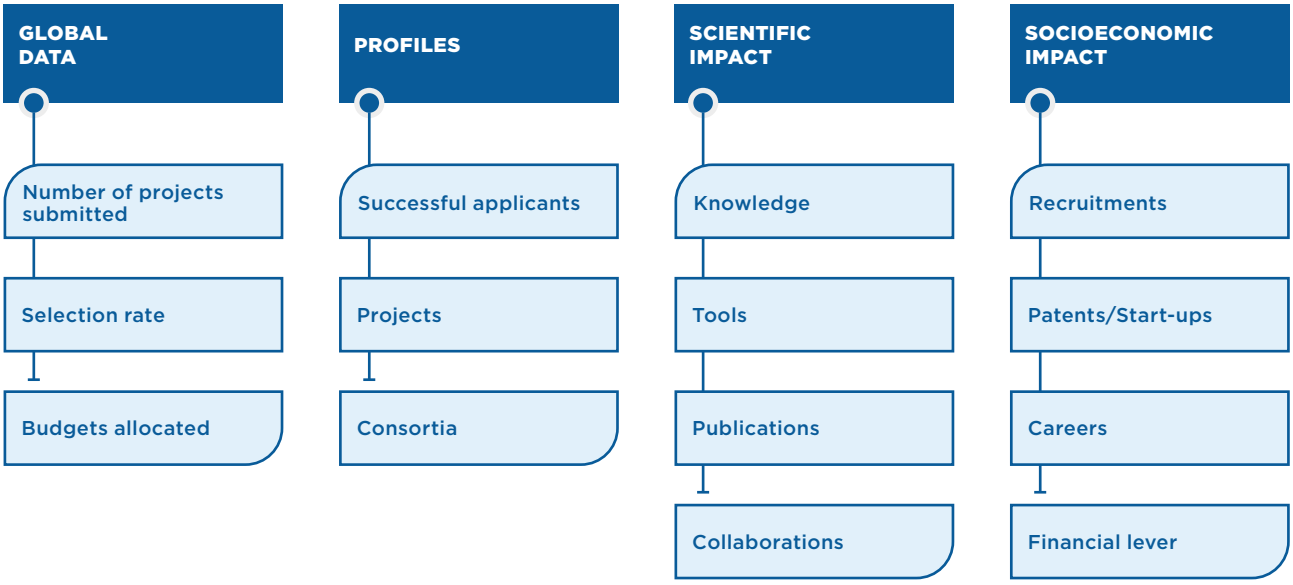
In parallel, the ITMO conducted an evaluation of the calls for proposals for which it was responsible for programming, once there was sufficient hindsight. These evaluations took place in two stages: the first being a meeting with the programme beneficiaries during feedback seminars; the second being the evaluation of the data from their projects and final reports, as well as from the reports of the selection committees.

The ITMO held 6 feedback seminars between 2014 and 2021, aimed at:

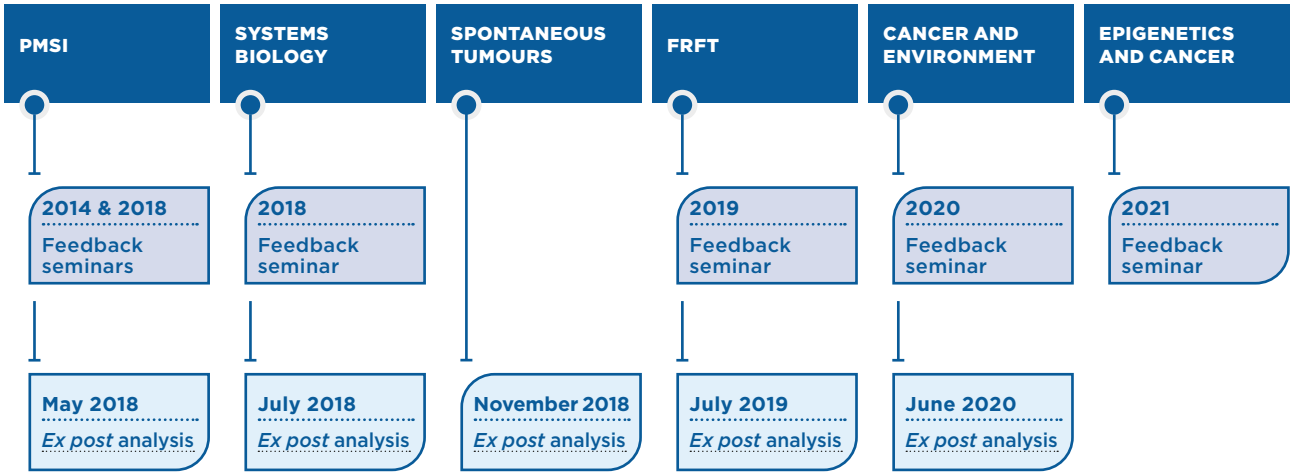
- examining the scientific or technological advances made within the framework of the programmes, thanks to presentations made by the project leaders;
- collecting the individual impressions of the beneficiary scientists regarding the contribution of the programmes to their research project and career;
- achieving an overview of the challenges still to be addressed and the new trends in the themes of the ITMO programmes, notably through the interactions promoted by the seminars.

Then, the ITMO analysed the data compiled for each of the programmes using an internally-developed grid containing descriptive elements and impact indicators.

A GENERIC GRID FOR EVALUATING THE PROGRAMMES



EVALUATION OF THE PROGRAMMES FROM 2018 ONWARDS



Supplemented by the teachings from the feedback seminars, the 5 *ex post* analyses carried out since 2018, available on the ITMO website, have made it possible to:

- determine whether a program had met its objectives, and to which actions of the Cancer Control Plans it had contributed;
- visualise the impacts of a programme, and therefore the budgets invested, in terms of scientific and technological progress made;
- identify elements indicating the need for a programme to evolve;
- provide data to the ITMO to advance its reflection on the main strategic orientations to adopt for cancer research.

The programme supporting the acquisition of equipment for cancer research, launched in 2016 in line with the orientations of the 3rd Cancer Control Plan and a recommendation issued by the INCa Scientific Advisory Board in 2015, was the subject of a special analysis: the ITMO recontacted the 2016-2019 beneficiaries in order to collect information on the equipment it had funded, and made this information available to the cancer community through a booklet available on its website and distributed in its bimonthly newsletter.

IDENTIFY THE EQUIPMENT FUNDED TO PROMOTE SHARING

Between 2016 and 2019, the Aviesan ITMO Cancer had funded 87 items of equipment, for a total cost of €13.7M. The equipment mainly belonged to the categories of 'Imaging', 'Cell characterisation and histology' and 'Biochemistry and proteomics'. A regional analysis shows that Île-de-France and Occitanie, and to a lesser extent Auvergne-Rhône-Alpes and Provence-Alpes-Côte d'Azur, accounted for the largest amount of equipment funded over the period.

A booklet listing these items of equipment, funded during the 4 calls for proposals of the 2016-2019 period, was produced, which:

- **describes their main characteristics and applications, and the environment in which they are installed;**
- **presents some findings obtained through their use;**
- **provides the necessary contacts for possible collaborations, in accordance with one of the major objectives of the programme.**

Long-term support for structural partner programmes

Alongside its own programmes, the Aviesan ITMO Cancer has contributed to several partner institution or organisation programmes through the funding of projects with a cancer dimension. The data from these partnerships are set out each year in INCa's annual scientific report *Actions for Cancer Research*.

PARTNERSHIP FIGURES FOR 2011-2021

This participation took place in several ways:

- funding of research projects in the environment field: between 2011 and 2021, the ITMO supported 50 cancer projects within the framework of the French Agency for Food, Environmental and Occupational Health and Safety (Anses) PNR-EST (Environmental and Occupational Health Research Programme). This major collaboration was the subject of a feedback seminar in 2018 and an *ex post* analysis in 2021, shared with Anses and published. In addition, 2 cancer-related projects were also funded in 2020 within the framework of the French Biodiversity Agency (OFB) Écophyto 2+ programme;
- support for young scientists in getting started: as part of the CNRS and Inserm joint Atip-Avenir programme (48 projects funded between 2011 and 2021) and, since 2020, as part of the French National Research Agency (ANR) Young Researchers (JCJC) programme, 3 projects funded between 2020 and 2021);

CANCER AND ENVIRONMENT: TWO-PRONGED SUPPORT

During the programming of its Cancer and Environment (K-Env) call for proposals, the Aviesan ITMO Cancer continued to support the Anses PNR-EST programme. In total, 75 projects on this theme were funded between 2012 and 2017, for a total amount of €23.3M.

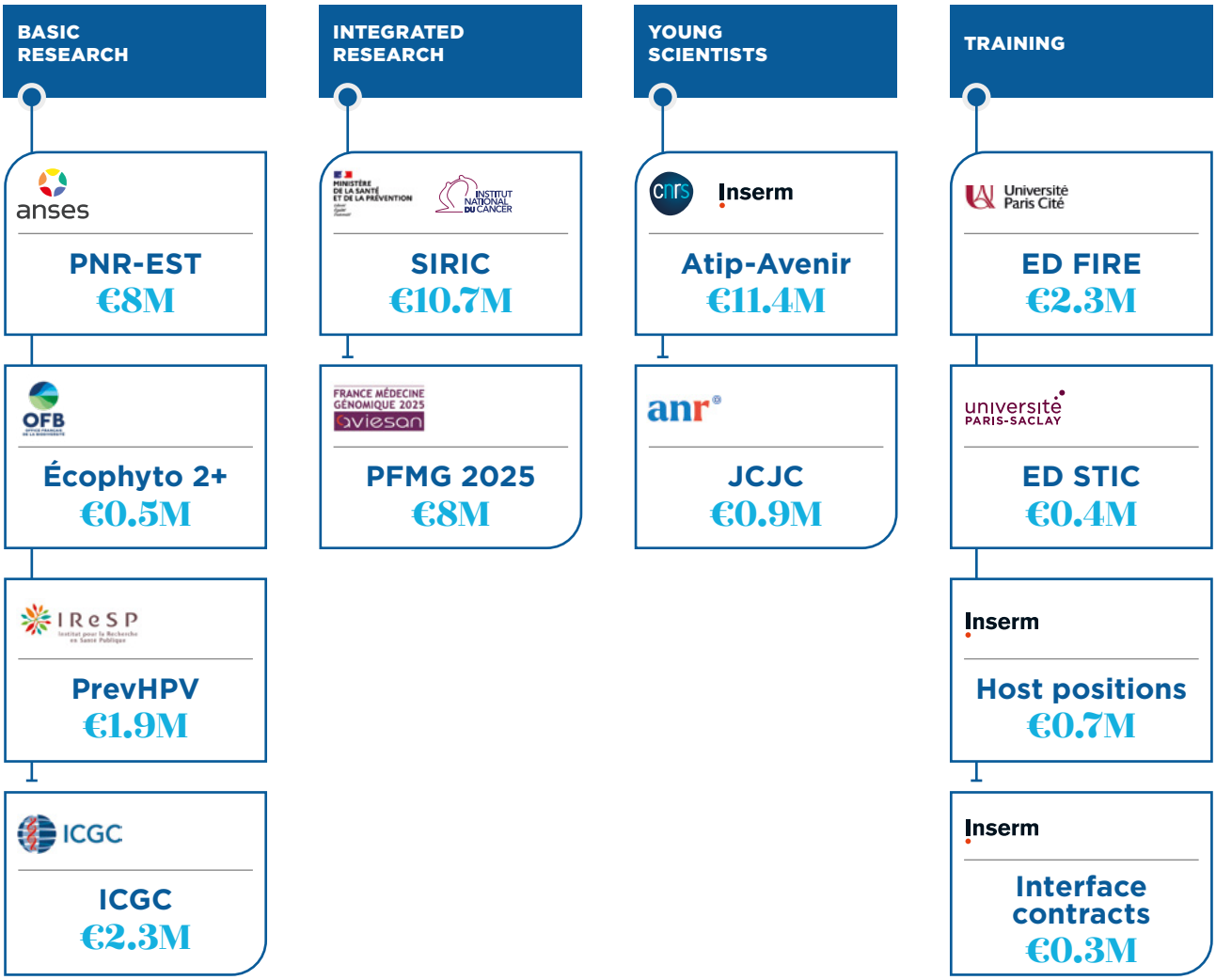
The *ex post* analysis of the two programmes over this period evaluated the merits of this two-pronged support by the Aviesan ITMO Cancer on the theme of Cancer and Environment:

- **the target communities of the two programmes were mostly distinct (with 75% of the PNR-EST beneficiaries not participating in K-Env);**
- **basic research was more predominant in K-Env (77% vs. 56%), while PNR-EST hosted more epidemiology (34% vs. 23%) and human and social sciences (10% of projects);**
- **although the study of chemical risk was predominant in both programmes, physical risk factors received 4 times more attention in K-Env (12% vs. 3%);**
- **although new tools were developed and mechanisms elucidated in both programmes, only PNR-EST led to descriptions of links between exposure and cancer, and provided socioeconomic elements;**
- **the fields of publication varied greatly in both programmes due to the multidisciplinary nature of the theme. However, K-Env resulted in 5 times more publications in generalist journals (35% vs. 7%), and PNR-EST in 3 times more publications in public health (23% vs. 8%), in line with the calls for proposals.**

A comparison of the indicators analysed revealed a high level of complementarity between the two programmes, particularly regarding the target communities and types of research conducted. This conclusion confirmed the relevance of the choice made by the Aviesan ITMO Cancer to launch its K-Env programme in parallel to its support for PNR-EST.

- the attribution of individual aid for training in and through research, in addition to its own FRFT(-Doc) programme:
  - > for the completion of an interdisciplinary doctorate relating to cancer, within the framework of the doctoral schools (DS) FIRE (Research and Education Innovation Frontiers, 22 research grants between 2011 and 2021) and STIC (Information and Communication Sciences and Techniques, 4 grants between 2018 and 2021),
  - > for the completion of a doctorate by young graduates in medicine, pharmacy, odontology and veterinary medicine, within the framework of the Inserm Host positions program (8 projects funded between 2014 and 2018),
  - > for funding the research of successful clinician applicants to the Inserm Hospital interface contracts programme (3 projects supported during the 2017-2018 period).

2011-2021 PARTNERSHIPS: STRONG SUPPORT FOR RESEARCH AND TRAINING



The ITMO has also occasionally been involved in funding several programmes of national and international scope:

- the network of Integrated Cancer Research Sites (SIRICs), alongside INCa and the General Directorate of Healthcare Provision (DGOS). Certified by INCa (8 in 2012 and 8 in 2018), the SIRICs are tasked with implementing multidisciplinary research programmes to accelerate the production of new knowledge and promote its dissemination and application in the treatment of cancer;
- the 2025 French Genomic Medicine Initiative (PFMG), driven by Aviesan, aimed at enabling cancer sufferers throughout the country to benefit equitably from new genomic medicine technologies for diagnosis, prevention and care: the ITMO contributed to the funding of the Multipli pilot project dedicated to cancer, and one of its directors is a member of the project's Steering Committee;
- the PrevHPV programme of the French Institute for Public Health Research (IReSP), interventional research on the acceptability of Human papillomavirus (HPV) vaccination among secondary school students: in 2019, the ITMO supported the consortium project formed during the call for expression of interest;
- the International Cancer Genome Consortium (ICGC), pooling global data from the whole sequencing of over twenty tumour types: the ITMO funded 6 of the 8 projects representing France's contribution to the ICGC (prostate cancer, Ewing sarcoma, retinoblastoma, gynaecological carcinosarcoma, leiomyosarcoma, B-cell prolymphocytic leukaemia).

Balanced distribution of funding

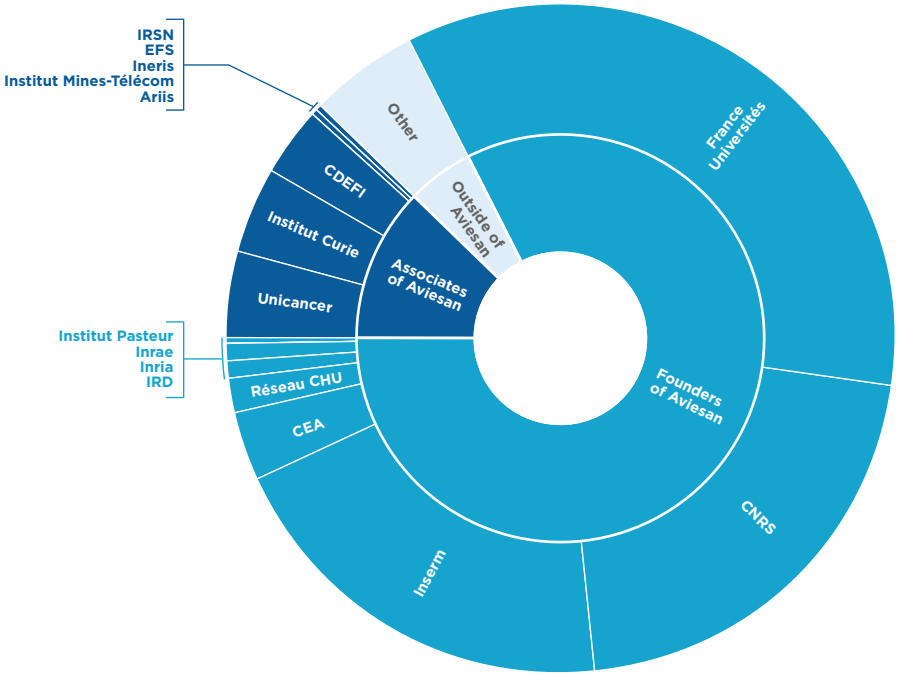
A data analysis conducted during the period of the 3rd Cancer Control Plan (2014-2019) shows that almost all of the funding granted by the ITMO as part of its programming and partnerships went to structures supervised by at least one member, founder or associate, of Aviesan.

The main beneficiary institutions, in terms of funding share and allocated budget, were members of France Universités (41 beneficiary universities), CNRS and Inserm, followed by CEA and members of the Réseau CHU. The associate members of Aviesan were also well represented, particularly (and logically) the members of Unicancer and Institut Curie, as well as engineering schools belonging to the Conference of Deans of French Schools of Engineering (CDEFI). This diversity of the institutions funded reflects the multidisciplinary nature of the ITMO's programming and, more generally, the cross-cutting nature of cancer research.

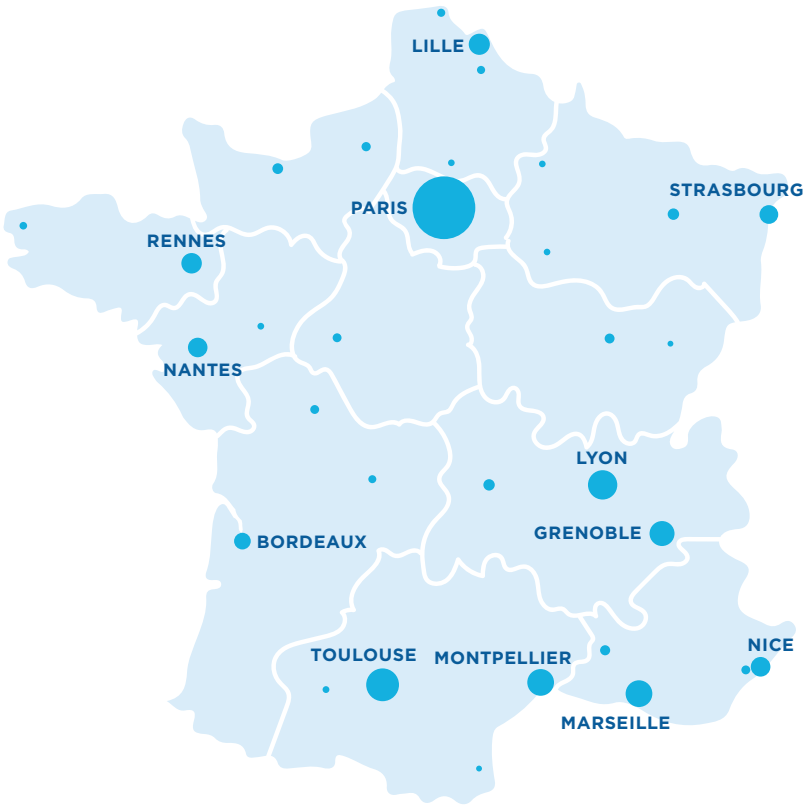
The structures funded during the aforementioned period were spread across France, albeit with 6 cities having greater representation: Paris, Toulouse, Lyon, Marseille, Montpellier and Grenoble.

The research centres that received the most funding were Institut Curie, Gustave-Roussy and the Cancer Research Centre in Lyon ●

MULTI-ORGANISATION FUNDING



... ACROSS FRANCE



04.

ITMO CANCER, A HISTORICAL ROLE IN ANIMATING THE CANCER RESEARCH COMMUNITY

The Aviesan ITMO Cancer conducts its facilitation mission through actions that federate the cancer community, both nationally and internationally. Between 2011 and 2021, it has led, alone or in collaboration, the setting up and management of interdisciplinary think tanks, as well as the organisation of various national meetings, focusing particularly on emerging themes stemming from its strategic orientations.

The ITMO has also developed two communication tools designed to inform the entire cancer community about its actions, notably in terms of programming, and about external events and calls for proposals, in France and Europe:

- a bimonthly newsletter, available on subscription, listing the calls for proposals, the calls for applications and the national and European colloquia, as well as opportunities for training and employment in France;
- a website, to learn more about the ITMO (positioning, missions, Expert Committee), its strategy (strategic orientations, contribution to the Ten-year Cancer Control Strategy), its calls for proposals (past and present), the results of the evaluation of its programmes (feedback seminars, *ex post* analyses), and its national and international facilitation actions.

INTERDISCIPLINARY THINK TANKS, PARTICULARLY TO SUPPORT PROGRAMMING

2017	**IMPACT ASSESSMENT**	• Define a concerted approach between funding providers from the public sector and associations to assess the impact of the research projects funded in cancer.
	EXPERIMENTAL MODELS	• Define the elements of a call for proposals dedicated to optimising the principles of the 3Rs (Replacement, Reduction and Refinement) in the use of animal models. > 1st edition of the 3Rs call for proposals in 2019.
2018	**PRE-NEOPLASIA**	• Define the outlines of a new research field dedicated to pre-tumoural biological processes and the emergence of precision preventive medicine. > National discussion seminar in 2018; 1st edition of the Pre-neoplasia call for proposals in 2019.
	SUBCELLULAR MAPPING' PFA	• Define the research areas of the 1st Aviesan Federative Programme (PFA) dedicated to the subcellular mapping of the cancer cell. > Subcellular mapping PFA call for proposals in 2019.
	PMSI	• Rework the PMSI call for proposals to attract more specialists in mathematics, chemistry and computer science. > Splitting of the PMSI programme into PCSI and MIC; 1st PCSI and MIC calls for proposals in 2019.
2019	**NACRe**	• Evaluate the 20 years of activity of the NACRe (Nutrition, physical activity, cancer, research) network. > Recommendations issued for the future of the network.
	EQUIPMENT	• Renovate the call for proposals. > New format of the Equipment call for proposals in 2021.
2021	**TUMOUR MICROENVIRONMENT**	• Prepare the elements of a new call for proposals dedicated to the microenvironment of poor prognosis cancers (MCMP), in line with one of the major challenges of the 2021-2030 Ten-year Cancer Control Strategy. > 1st edition of the MCMP call for proposals in 2022.

NATIONAL MEETINGS TO BRING THE CANCER COMMUNITY TOGETHER

DATES	THEMES
17 December 2013	Radiobiology in Medicine
19 June 2015	FdV (Frontiers of Life Sciences) Thematic Day: New Insights in Cancer Research
26 June 2015	Atip-Avenir programme funding recipients with a project on the theme of cancer
02 October 2018	Feedback on the Environmental and Occupational Health Research Programme (PNR-EST): Occupational or environmental exposures and cancer risk
28 November 2018	National discussion seminar on the characterisation of preneoplastic lesions
06 March 2020	Launch of the 1st Aviesan federative programme: Subcellular mapping

INTERNATIONAL COLLOQUIA ON PRIORITY THEMES

DATES	THEMES
16 September 2011	The tumour cell and its microenvironment - Inaugural colloquium
13 November 2012	Cancer research and innovations - 4th R&D International Dating
17 June 2014	Epigenetics for novel therapeutic strategies - Continuation of the 4th R&D International Dating
9-10 November 2016	Toward next generation nanomedicine addressing cancer complexity
28 February 2017	Mathematical modelling of tumour heterogeneity in tumoral environments
27-28 November 2017	Cancer immunotherapy: Progresses & Challenges
06 February 2018	Immuno-oncology - 8th R&D International Dating
16 May 2018	14th ICGC Scientific workshop
16-18 June 2021	Fundamental research in pediatric cancer

The ITMO also promotes French public research abroad, through the organisation of international colloquia. Close to 10 colloquia took place between 2011 and 2021, with the majority in partnership with INCa. The ITMO also co-organised, with the French Health Industry Alliance for Research and Innovation (Ariis), the 4th and 8th R&D International Dating, aimed at promoting interactions between public research and the competent industry in the field of cancer. Finally, the ITMO held a stand from 2017 to 2019 at the annual meeting of the American Association for Cancer Research, the largest global meeting on basic cancer research.

In 2020, the European Union Mission on Cancer asked the ITMO for feedback regarding the reactions of the French cancer community to its progress report: *Conquering Cancer: Mission possible*. To do this, the ITMO conducted a survey of the directors of the structures involved in cancer research and of the members of its committee.

This feedback, as well as its own reflection, were summarised in the document *Position Paper on the EU Mission on Cancer report* 'Conquering Cancer: Mission Possible', which was published on its website.

In 2021, the ITMO got involved, alongside INCa and the French Ministry of Higher Education, Research and Innovation (MESRI), in the French-led application for the preparatory call for the implementation of UNCAN.eu. A recommendation of the EU Mission on Cancer and a component of the European Cancer Plan, the UNCAN.eu initiative aims to drive basic cancer research at the European level. The French-led project was selected by the European Commission in 2022 •

A PRESENCE AT THE AACR TO SHOWCASE FRENCH ASSETS

From 2017 to 2019, the Aviesan ITMO Cancer held the 'Cancer Research in France' stand at the annual meeting of the American Association for Cancer Research.

Its purpose was to:

- **inform the community of French or foreign young researchers of funding possibilities in France;**
- **inform foreign scientists of the possibilities for collaboration and funding of collaborations with French laboratories;**
- **provide access to documents collected from laboratories, *Cancéropôles*, etc., presenting:**
  - **> French institutions and laboratories,**
  - **> funding, mobility and team creation initiatives,**
  - **> offers of employment and mobility,**
  - **> future colloquia to take place in France.**

○ FRENCH NATIONAL ALLIANCE FOR LIFE SCIENCES AND HEALTH ○ **IMPROVING KNOWLEDGE IN LIFE SCIENCES AND HEALTH** ○

- Cancer
- Cell biology, development and evolution
- Genetics, genomics and bioinformatics
- Health technologies
- Immunology, inflammation, infectiology and microbiology
- Molecular and structural bases of life sciences
- Neurosciences, cognitive sciences, neurology, psychiatry
- Pathophysiology, metabolism and nutrition
- Public health

aviesan

8, rue de la Croix-Jarry
75013 Paris
France

aviesan.fr

Publication Director: Gilles Bloch – Design and drafting: Emmanuelle Chollet, Muriel Altabef
Artistic leadership: Myriem Belkacem - Creation and production: Kazoar – ISBN: 978-2-85598-931-0 – Legal deposit: October 2022.