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INSTITUT NATIONAL DU CANCER

SCIENTIFIC REPORT

2022

ACTIONS FOR CANCER RESEARCH

The French National Cancer Institute is the health and science agency in charge of cancer control.

Working group

Scientific coordination
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INTRODUCTION

ACTIONS FOR CANCER RESEARCH

INSTITUT NATIONAL DU CANCER

SCIENTIFIC REPORT 2022

2022 was a challenging year for actions supporting cancer research in France with the increased pace in implementation of the Ten-Year Cancer Control Strategy.

The Ten-Year Cancer Control Strategy was launched in 2021 by the French President with the aims of improving cancer prevention, reducing cancer sequelae, fighting against poor prognosis cancers, and ensuring everyone benefits from progress.

Last year, I said that the Strategy marked the beginning of a new chapter in the national fight against cancer — a chapter that should lead to significant progress in all areas likely to reduce cancer and improve patients' quality of life during and after the disease.

Indeed, research and innovation are pivotal in the efforts needed to achieve these objectives.

In 2022, one year on, the implementation of the Strategy's actions provides a promising picture. These actions are now being carried out at a steady pace. Specific and innovative actions supporting research projects and the structuring of research have been launched in all disciplines and fields, including prevention, sequelae, and poor prognosis cancers. They have been funded with new and specific budgets through thematic calls for proposals, programme designations, tools, and networks.

Moreover, the Strategy is strengthening core national cancer research actions. Hence, for example, more funding has significantly been poured into INCa's recurrent main research programmes, namely the Biology and basic sciences for cancer research programme PLBIO and the National clinical research programme on cancer PHRC-K.

All this activity has reinforced the need to evaluate the impact of not only the Ten-year Cancer Control Strategy, but also overall public support of cancer research actions. In fact, an evaluation strategy has been requested and is now being developed.

This 2022 Scientific report reflects the efforts in implementing the Ten-Year Cancer Control Strategy and conducting core cancer research actions. At the same time, beyond that, support for cancer research and innovation has continued to remain open to emerging ideas and topics in cancer research, to new fields for scientific knowledge, aiming at providing new opportunities for researchers and, eventually, patients and individuals. In this Scientific report, the strategic orientations for advancing cancer research include new actions intended to be conducted in the coming years.

Prof. Norbert IFRAH, MD
President of the
French National Cancer Institute

LIST OF ABBREVIATIONS

ACTIONS FOR CANCER RESEARCH

INSTITUT NATIONAL DU CANCER

SCIENTIFIC REPORT 2022

ACSÉ: Programme d'accès sécurisé à des thérapies ciblées innovantes (Secured Access to innovative therapies programme)

ADEME: Agence de la transition écologique (French Agency for ecological transition)

ANR: Agence nationale de la recherche (French National Research Agency)

ANRS MIE : Agence nationale de recherche sur le sida, les hépatites virales et les maladies infectieuses émergentes (French National Agency for research on AIDS, Viral Hepatitis Research and Emerging Infectious Diseases)

ANSES: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (French National Food, Environment and Occupational Health Safety Agency)

AVIESAN: Alliance nationale pour les sciences de la vie et de la santé (French National Alliance for Life Sciences and Health)

BCB: Bases de données clinico-biologiques (Clinical and Biological Databases)

CAR-T: Chimeric Antigenic Receptor T

CLIP²: Centres labellisés de phase précoce (Early-phase clinical trial centres)

CMR: Carcinogenic, Mutagenic and Reprotoxic

CNAM: Caisse nationale d'assurance maladie (French National Health Insurance Fund)

CPE: Cancer Prevention Europe

CSO: Common Scientific Outline of the international cancer research partnership ICRP

DGOS: Direction générale de l'offre de soins (Directorate of Health Care, in the French Ministry of Health)

DMP: Data Management Plan

HCERES: Haut conseil de l'évaluation de la recherche et de l'enseignement supérieur (French High Council for Evaluation of Research and Higher Education)

HCP: Health Cloud Platform

HSS: Human and Social Sciences

HSS-E-PH: Human and Social Sciences – Epidemiology – Public Health

IARC: International Agency for Research on Cancer

ICF: Informed Consent Forms

IMI: Innovative Medicines Initiative

INCA: Institut national du cancer (French National Cancer Institute)

INSERM: Institut national de la santé et de la recherche médicale (French National Institute of Health and Medical Research)

IRESP: Institut pour la recherche en santé publique (Institute for Public Health Research)

ITMO (-AVIESAN): Institut thématique multi-organisation (theme-based Multi-Organisation Institute for Cancer)

MCMP: Programme microenvironnement des cancers de mauvais pronostic (Poor prognosis cancer microenvironment research programme)

MIC: Programme pour la contribution des mathématiques et de l'Informatique à l'oncologie (mathematics and computer science contribution to oncology programme)

NGS: Next Generation Sequencing

OSIRIS: Groupe inter-siric sur le partage et l'intégration des données clinico-biologiques en cancérologie (French group on the sharing and integration of clinico-biological data in oncology)

PCSI: Programme pour la contribution de la physique, de le chimie et des sciences de l'Ingénieur à l'oncologie (Physics, Chemistry, and engineering Sciences contribution to oncology programme)

PH: Public Health

PHIR: Population Health Intervention Research

PHRC-K: Programme hospitalier de recherche clinique en cancérologie (French national programme for hospital clinical research on cancer)

PLBIO: Programme pour les projets libres de recherche en biologie du cancer (the Biology and basic sciences for cancer research programme)

PMSI: Programme pour la contribution de la physique, des mathématiques et des sciences de l'Ingénieur à l'oncologie (Physics, Mathematics and engineering Sciences related to cancer)

PRT-K: Programme de recherche translationnelle en cancérologie INCa-DGOS (French National clinical research programme on cancer)

SAB: Scientific Advisory Board

SIRIC: Site de recherche intégré sur le cancer (cancer integrated cancer research site)

WGPC: Working Group of Patients and Caregivers

WP: Work Package

TABLE OF CONTENTS

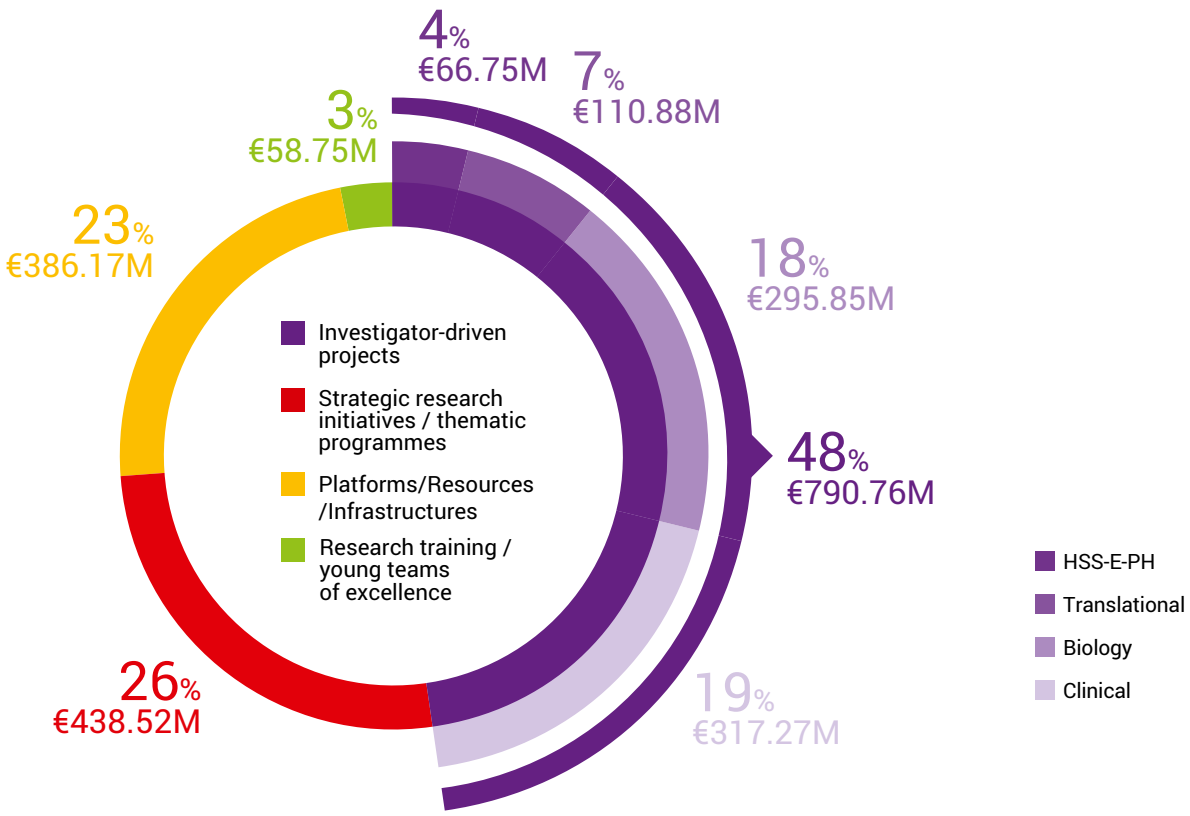
ACTIONS FOR CANCER RESEARCH

INSTITUT NATIONAL DU CANCER

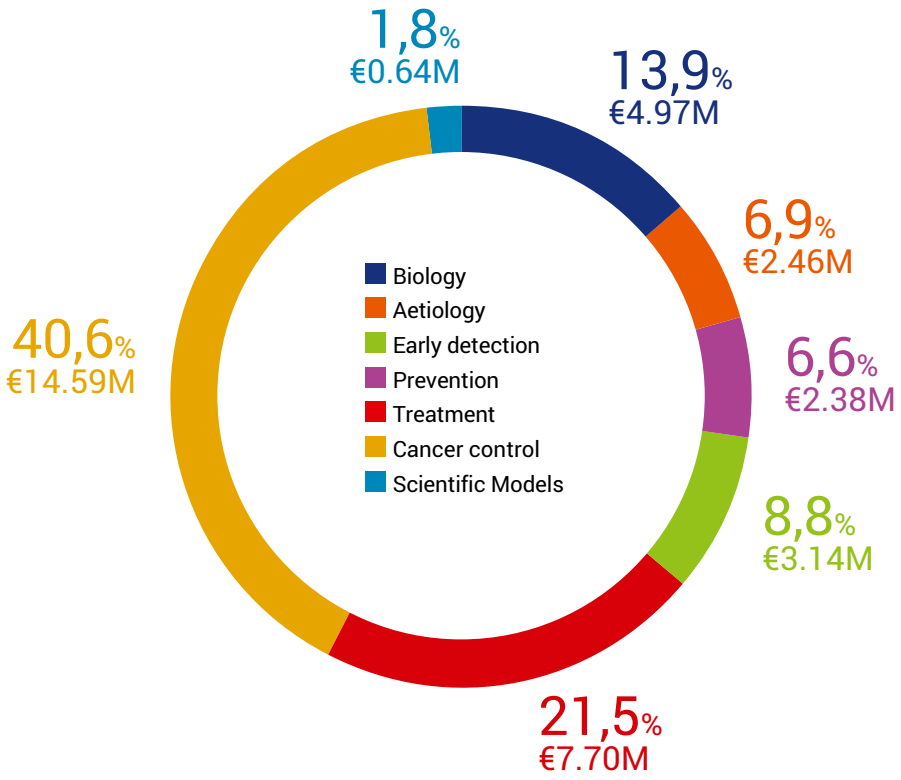
SCIENTIFIC REPORT 2022

ACTIONS FOR CANCER RESEARCH

2007-2022 multi-year cancer research funding by programme type: €1.67Bn invested



2021-2022 ten-year cancer control strategy's funding of cancer research : €35.89M invested



1

The international scientific advisory board

This 17th report to INCa's international Scientific Advisory Board (SAB) reviews actions carried out both by INCa and Aviesan's Multi-Organisation Thematic Institute for Cancer (ITMO Cancer-Aviesan). This report is the key element for SAB members to review the actions undertaken and subsequently advise and guide the Institute during its structuring processes and its initiatives.

Composed of internationally renowned experts and appointed by the supervising Ministers, INCa's Scientific Advisory Board:

- ensures that INCa's scientific and medical policy is consistent;
- reviews INCa's annual scientific report before it is presented to the Board of Directors;
- makes recommendations and provides opinions on INCa's scientific strategies and their implementation.

The first part of this report is focused on the 2022 recommendations of INCa's SAB. The SAB's recommendations are central to the Institute establishing an action plan and proposing a strategy to handle cancer research challenges over the years.

THE INTERNATIONAL SCIENTIFIC ADVISORY BOARD MEMBERS

The members of the Scientific Advisory Board are:

- **Dr. Geneviève Almouzni**, PhD, Institut Curie, Paris, France
- **Mrs. Pascale Altier**, VBO Consulting, Saint-Rémy-Lès-Chevreuse, France
- **Prof. Cécile Badoual**, MD, PhD, Hôpital Européen Georges Pompidou, Paris, France
- **Dr. Jean-Pierre Bizzari**, MD, Celgene, Summit, USA
- **Prof. Cédric Blanpain**, MD, PhD, Université Libre de Bruxelles, Brussels, Belgium
- **Dr. Franck Bourdeaut**, MD, PhD, Institut Curie, Paris, France
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- **Prof. Yann Gauduel**, PhD, Ecole Polytechnique – ENS Techniques Avancées, Palaiseau, France
- **Dr. Ivo G. Gut**, PhD, Centro nacional de analisis genomica (CNAG), Barcelona, Spain
- **Dr. Mette Kalager**, MD, PhD, Harvard T.H. Chan School of Public Health, Boston, USA
- **Prof. Catherine Lacombe**, MD, PhD, Institut Cochin, Paris, France
- **Dr. Douglas R. Lowy**, MD, NCI Acting Director, Bethesda, USA
- **Prof. Marc-André Mahé**, MD, PhD, General Director, Centre François Baclesse, Caen, France
- **Prof. Dame Theresa Marteau**, PhD, University of Cambridge, Cambridge, United Kingdom
- **Dr. Patrick Mehlen**, PhD, Centre de recherche en cancérologie de Lyon, Lyon, France
- **Prof. Stefan Pfister**, MD, German Cancer Research Centre (DKFZ), Heidelberg, Germany
- **Prof. Louise Potvin**, PhD, Institut de recherche en santé publique de l'Université de Montréal, Université de Montréal, Montreal, Canada
- **Ms. Fabienne Renaud**, Europa Donna France, Nantes, France
- **Prof. Gérard Socié**, MD, PhD, Hôpital Saint Louis, Paris, France
- **Dr. Naomi Taylor**, MD, PhD, National Cancer Institute, NIH, Bethesda, USA
- **Prof. Robert A. Weinberg**, PhD, Massachusetts Institute of Technology (MIT), Cambridge, USA
- **Prof. Laurence Zitvogel**, MD, PhD, Gustave Roussy, Villejuif, France

2022 RECOMMENDATIONS

1 The SAB is very impressed with the growth of the quality, breadth and excellence of cancer research in France over the past decade, in no small part due to the leadership of the INCa.

2 The SAB thanks Alain Eychène for his leadership in INCa the past 3 years and welcomes Bruno Quesnel.

3 Congratulations on the start of the new 10-year cancer plan – the SAB in particular is pleased to see:
- 80/234 measures are already launched
- Additional funding received from the French Government to support this work. It is important to stress that funding of cancer research is not an expense – it is an investment into a healthier future for French citizens.

4 New calls for proposals should be routinely linked back to the strategy.

5 Future annual reports should be structured to reflect the strategy's priorities (in particular for prevention-related efforts).

6 It is important to evaluate the impact and outcome of strategic initiatives, focused funding calls and open investigator-initiated research programs. When a new programme is launched, metrics and timing of evaluation(s) must also be made explicit and be related to the programme objectives.

7 Additional comments about specific research areas/programmes:
- overweight and obesity, important risk factors for 13+ cancers, are an increasing problem reaching epidemic proportions in European countries, including France – so it is exciting to see early investments in this area, however more is needed. A comprehensive approach to this and other priority areas is recommended;
- participation of the INCa in the Cancer Grand Challenges is endorsed by the SAB;
- in order to ensure that new technologies in France are developed, adopted, and spread based on the best evidence, INCa investment should be focused on addressing gaps most likely to inform practice and policy.

8 For your consideration: highlighting key research outcomes from INCa investments (publications, patents, clinical trials) each year that are helping to move towards the Cancer Strategy Goals. This communication could target the public and the science community.

9 Streamlining opportunities:
- combining calls for proposals on similar thematic topics into one is to be encouraged where logical (e.g. HSS-E-PH + PHIR);
- using the ERC selection process to fund highly ranked but not-ERC-funded candidates, particularly, at the ERC Starting Grant level.

2

2022 Cancer Research Activity

In recent years, the research and health landscape in oncology has undergone a major upheaval, giving France major opportunities to strengthen its innovative programmes while making it possible to initiate new ones. In the last few years, INCa has established a highly proactive policy, recognised by European and American colleagues, to expand collaboration in cancer research and to provide access to targeted therapies for patients identified as candidates through molecular tests.

INCa has a preeminent role in France with a national mandate encompassing all activity areas of value in the cancer control chain, from research to prevention and screening, to the organisation of cancer care and information for patients and their relatives.

Every year, INCa issues calls for investigator-driven proposals to the scientific community in the 4 main research areas: cancer biology, translational research, clinical research, and research in human and social sciences, epidemiology, and public health. The Institute supplements its cancer research support through specific actions and allocations to support cancer research structuring and strategic research initiatives, such as fostering precision medicine, to promote access to innovation for all patients.

Moreover, ITMO Cancer-Aviesan supplements cancer research support thanks to specific and thematic programmes aimed to support emerging fields, multidisciplinary projects, and basic and translational cancer research training.

The following section presents a detailed review of the research programmes conducted in 2022.

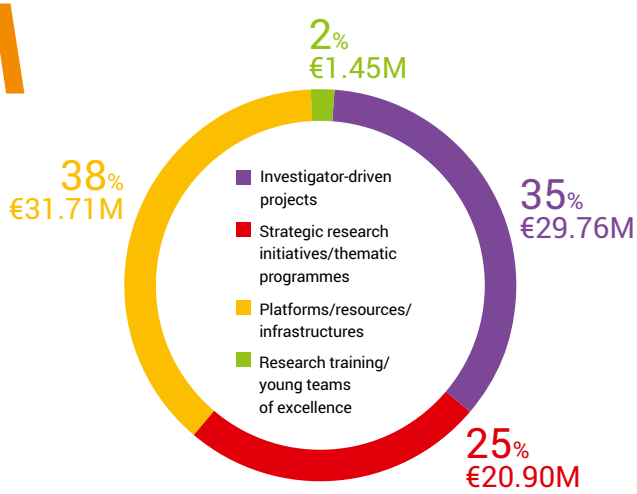
BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH

Research focused on cancer biology helps to increase the basic knowledge on oncogenesis and on the development and progression of cancer. The understanding of biological mechanisms opens up new prospects for advances in treatment, inhibition of resistance mechanisms, and the development of tools through the establishment of projects involving physics, mathematics, or information technology.

In order to promote and support this progress in the long term, INCa launches a recurrent call for proposals, focused on cancer biology and basic sciences, supplemented by thematic calls for proposals programmed by ITMO Cancer-Aviesan in order to strengthen and support emerging and priority cancer research areas.

In 2022, support for biology and basic sciences for cancer research amounted to:

€83.82M



The biology and basic sciences for cancer research programme PLBIO

Since 2005, INCa has issued a call for investigator-driven proposals to the French scientific community for the funding of original and promising projects in different areas and disciplines of basic research in oncology.

In 2022, 51 projects were selected for funding out of the 224 proposals submitted for a total amount of €29.8M (22.8% of the submitted applications were selected for funding).

TABLE 1
FEATURES OF THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2022

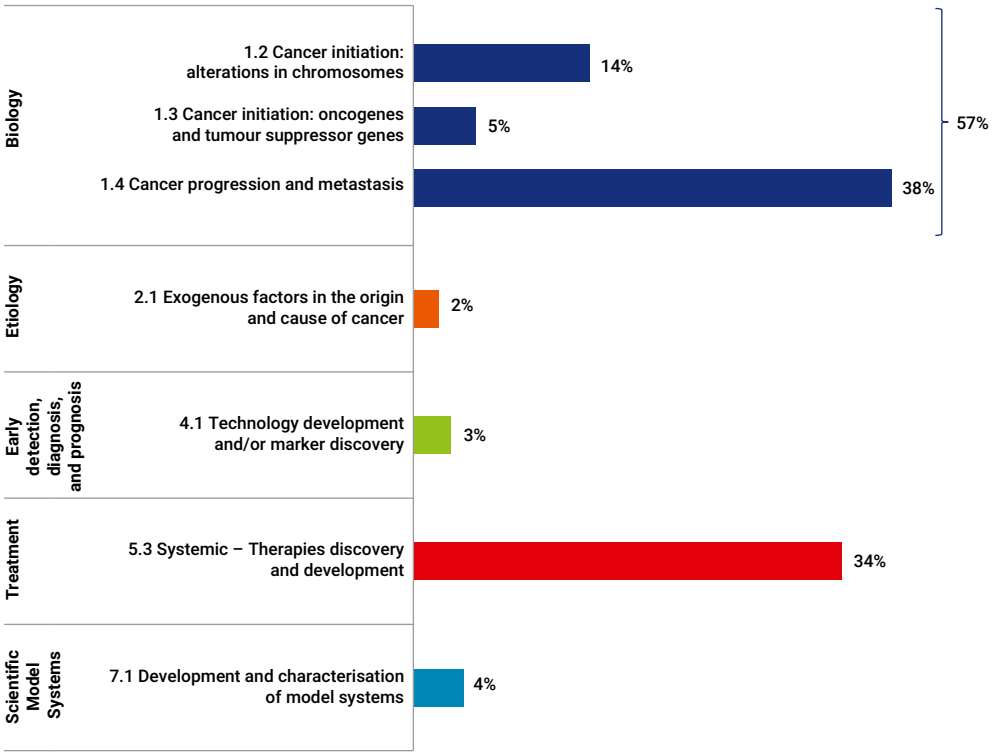
Objectives	To expand our understanding of cancer and develop new tools to create new therapeutic approaches. Open to all areas of basic research and to scientific disciplines involved in tumour biology research, this call was launched to: • Enable the achievement of original projects; • Strengthen multidisciplinary collaborations; • Develop research in emerging areas.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€29.8M**
Proposals submitted	**224**
Projects selected	**51**
Selection rate	**22.8%**

Figure 1 presents a detailed analysis of the projects selected for funding:

- most of the funded projects (57%) are aimed at studying the biological mechanisms of cell transformation and disease progression, according to the international CSO classification[1] (CSO 1). Of these, 38% of the projects focus on the interaction between tumour cells and their microenvironment (cell mobility, tumour invasion, metastasis, cancer stem cells, immunological microenvironment, or angiogenesis, CSO 1.4). This category is well represented every year. This trend reflects the interest of these research fields in cancer biology;
- 34% of the funded projects are aimed at studying either the molecular mechanisms of response and resistance to treatments, or at identifying new therapeutic targets (CSO 5);
- 4% of the funded projects concern research into model systems (CSO 7);
- 3% of the funded projects concern the early detection, diagnosis, and prognosis of cancers (CSO 4);
- 2% of the funded projects relate to cancer aetiology (CSO 2).

1. The detailed description of the CSO classification is presented in Appendix 1.

FIGURE 1
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE BIOLOGY AND BASIC SCIENCES FOR CANCER RESEARCH PROGRAMME IN 2022



2022:
51 projects selected for a total amount of €29.8M

Figure 2 depicts a detailed analysis of the research topics of the selected projects. Some topics are particularly well represented:

- cell signalling: 23% of the funded projects, with a particular emphasis on cellular metabolism (20%) and cell death (20%);
- tumour microenvironment: 22% of the funded projects, with a majority of projects addressing the role of tumour-associated macrophages and tumour-infiltrating lymphocytes (34%) and cell-cell communication in the microenvironment (20%);
- pharmacology: 16% of the funded projects with most projects dealing with drug resistance (43%);
- immunology: 15% of the funded projects, with a huge focus on immune surveillance or mechanisms of escape from immune surveillance (63%). It is also worth noting that several projects focus on immunotherapy investigation (21%);
- genetics: 14% of the funded projects. 27% of these projects study genetic mutations and 24% DNA damage.

FIGURE 2
ANALYSIS OF THE MAIN RESEARCH TOPICS STUDIED BY THE PROJECTS FUNDED IN 2022 AND THE DISTRIBUTION OF THE RESEARCH FIELDS INTO THESE MAIN TOPICS

Setting up the immuno-oncology webinar series sponsored by French National Cancer Institute and the National Cancer Center of Japan (NCC)

国立研究開発法人
国立がん研究センター
National Cancer Center Japan

The close collaboration between France and Japan in relation to cancer has been further strengthened by a memorandum of understanding signed by INCa and the National Cancer Center of Japan. In this way, in December 2019, INCa and the NCC of Japan jointly organised a workshop on paediatric cancer.

To keep up the momentum of this collaboration, INCa and the NCC of Japan, together with the French Embassy have been discussing the opportunity of jointly organising another scientific event. The pandemic context even fuelled their desire to offer a more meaningful format:

The French National Cancer Institute and the National Cancer Center of Japan, with support from the Office for Science and Technology of the French Embassy to Japan, have organised a series of webinars focusing on immuno-oncology throughout 2022. These webinars are also supported by the Kiyoko Goto and Paul Bourdarie Cancer Foundation:

- **immune checkpoint inhibitors and beyond (January 2022)** – Dr. Hiroyoshi Nishikawa I Prof. Daniel Olive;
- **cell therapy against cancer (March 2022)** – Dr. Yuki Kagoya I Dr. Sebastian Amigorena;
- **anti-cancer vaccines and eradication of chronic inflammation (May 2022)** – Prof. Masanori Hatakeyama I Prof. Eric Tartour;
- **tumour immune microenvironment (June 2022)** – Prof. Osamu Takeuchi I Prof. Karin Tarte.

These webinars have provided an opportunity for French and Japanese researchers to present their work. These webinars will conclude with a workshop in Tokyo, in January 2023.

Both Institutes are keen to develop, build and further strengthen the close collaboration between the two nations in many areas of cancer research and clinical activities.

Thematic cancer research programmes by ITMO Cancer-Aviesan

POOR PROGNOSIS CANCER MICROENVIRONMENT RESEARCH MCMP PROGRAMME

The general objective of the "Microenvironment of poor prognosis cancers", MCMP, call for proposals is to fund interdisciplinary or multi-intradisciplinary projects allowing the functional characterisation of the microenvironment of cancers for which therapeutic options lack efficacy, and which are characterised by a standardised net 5-year survival rate of less than 33%. This programme is in line with one of the key objectives of the Ten-Year Cancer Control Strategy by targeting cancers with a poor prognosis.

Four research focus are proposed:

- high-definition spatiotemporal characterisation of the microenvironment, leading to a functional study;
- high definition decoding of cellular networks and local signalling;
- reprogramming of the tumour microenvironment;
- development of in vitro or ex vivo models, reproducing the spatiotemporal evolution of the tumour/microenvironment pair.

TABLE 2
FEATURES OF THE MCMP PROGRAMME IN 2022

Objectives	To better understand the role of the tumour microenvironment in the development of cancers for which therapeutic options lack efficacy, and which are characterised by a standardised net 5-year survival rate after diagnosis of less than 33%.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€4.3M**
Proposals submitted	23
Projects selected	**7**
Selection rate	30%

All projects funded in 2022 belonged to the immuno-oncology domain. Several were aimed at unravelling the mechanisms underlying the protumoural effects of the tumour microenvironment:

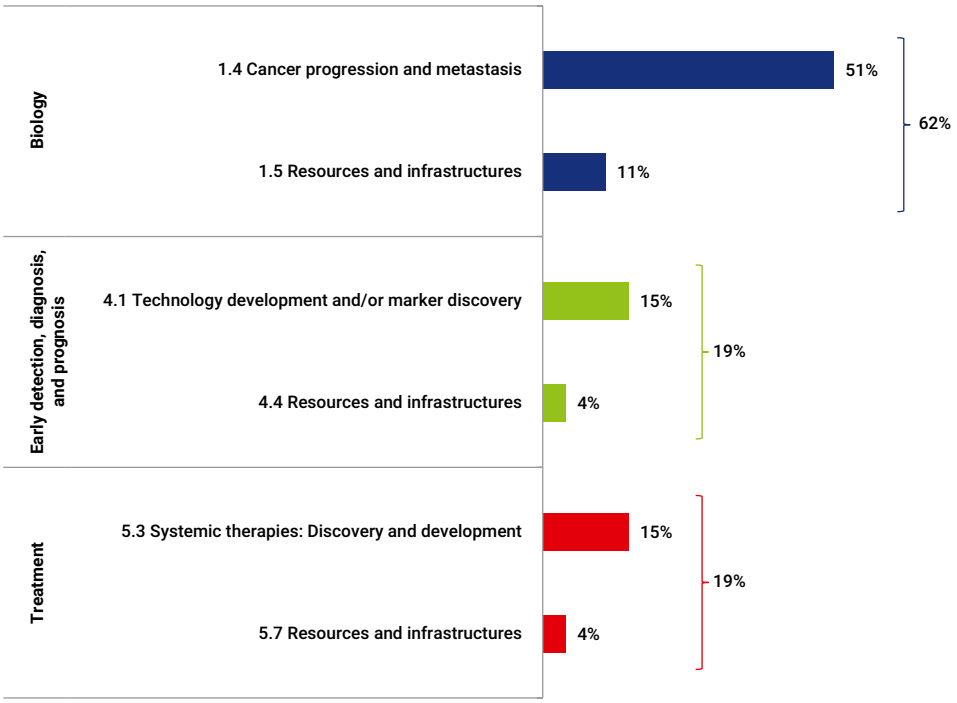
- impact of the cells of the microenvironment (tumour-associated macrophages (TAMs), fibroblasts, CD207+ DC2 dendritic cells) or of the extracellular matrix on T lymphocyte mobilisation and activity (non-small cell lung carcinoma, malignant pleural mesothelioma, digestive – namely pancreatic – carcinomas);
- impact of immunosuppressive myeloid cells on tumorigenic, metastatic and resistance properties of circulating cancer stem cells (gastric cancer).

Other projects looked at the impact of chemotherapies on the tumour immune microenvironment and its modulation by the inhibition of histone-deacetylases in gastric cancer; the characterisation of cellular networks and microbial or metabolic signals in the microenvironment of hepatocellular carcinoma.

The projects were all based on patient samples, as well as animal models (including xenografts) or cocultures (including spheroids). They included single-cell (and single-nucleus) RNA sequencing, high-resolution imaging, multiomics (spatial transcriptomics, matrisome and microbiome), mathematical modelling and bioinformatics.

FIGURE 3

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE MCMP PROGRAMME IN 2022 ACCORDING TO THE CSO CLASSIFICATION



Ex post analysis of the Research Projects in Epigenetics and Cancer Programme

This analysis was carried out in March 2022. It covered the entire programming period, from 2013 to 2015. A feedback seminar organised in October 2021 with former laureates of the programme and members of the selection committees enriched this analysis. The *ex post* analysis shows that the projects supported addressed most of the factors known at the time to be involved in epigenetic mechanisms, as well as other mechanisms for regulating gene expression. The projects led to the development of several tools and models, as well as to scientific advances that extended beyond the field of oncology in some cases.

INTERDISCIPLINARY APPROACHES TO ONCOGENIC PROCESSES AND THERAPEUTIC PERSPECTIVES: PHYSICS, CHEMISTRY, AND ENGINEERING SCIENCES CONTRIBUTION TO ONCOLOGY PCSI PROGRAMME

Initiated in 2019 following the redesign and split of the previous PMSI programme (physics, mathematics and engineering sciences related to cancer), the PCSI (Physics, chemistry, and engineering sciences) programme aims to improve understanding of cancer diseases and improve cancer prognosis by funding projects based on concepts or tools from physics, chemistry or engineering sciences. It allows funding of both proof-of-concept (PoC) projects and full projects.

TABLE 3
FEATURES OF THE PCSI PROGRAMME IN 2022

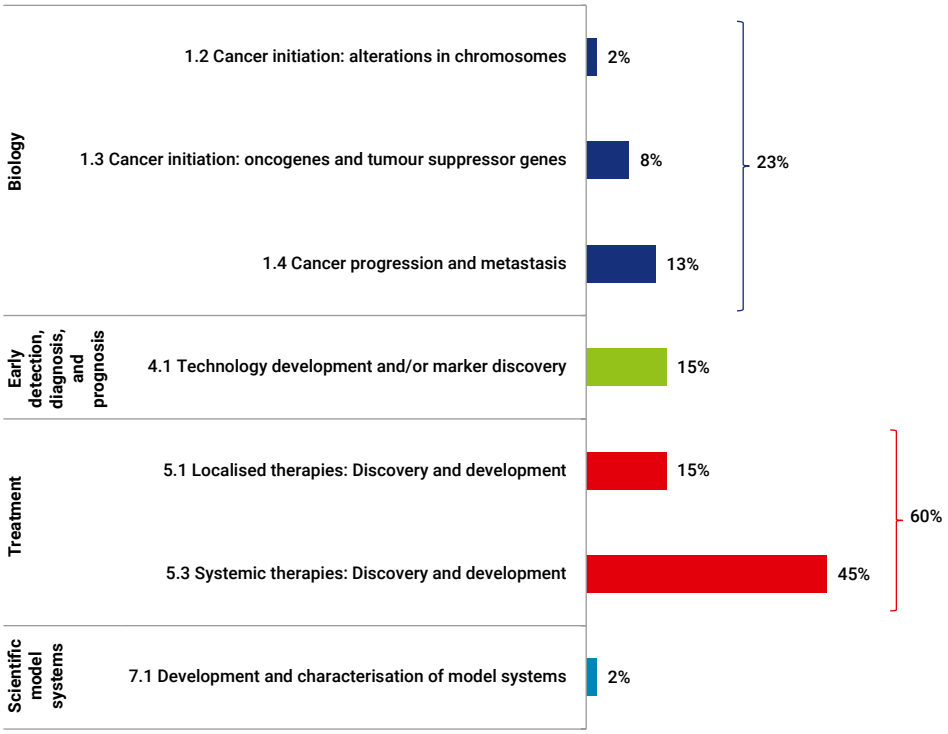
Objectives	To improve understanding of cancer diseases and improve the prognosis of patients thanks to concepts or tools from physics, chemistry or engineering sciences.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€8.1M**
Proposals submitted	**92**
Projects selected	**31 (15 PoC & 16 Full)**
Selection rate	**34%**

The projects funded in 2022 fall into 3 main categories:

- study of mechanisms involved in carcinogenesis:
  - metabolism of fatty acids and cholesterol in prostate cancer cells,
  - role of sphingomyelin metabolism in the formation and maintenance of invadopodia, involved in the invasive function of breast cancer cells,
  - impact of lactate accumulation and acidification on the intracellular metabolism of cancer cells,
  - interactions between acute lymphoblastic leukaemia T-cells and thymic epithelial cells,
  - mechanisms whereby phosphorylation and liquid-liquid phase separation regulate the binding of BRCA2 to its partners,
  - biogenesis of promyelocytic leukemia body (PML) nuclear bodies and association between their dynamics and structure with their antitumour functions,
  - nature and role in tumour infiltration of proteins involved in the detection of nanotopographic variations by macrophage podosomes,
  - impact of the mechanical properties of the glioblastoma cell nucleus on invasiveness and identification of potential therapeutic targets,
  - contribution of transcription and DNA repair combined with exposure to mutagens to mutational processes in human cancers;

- methods development for studying or treating cancer:
  - study of the mechanical properties of the microenvironment of pancreatic adenocarcinomas on suspended micro-tissue,
  - in vitro and in vivo comparison of two nucleic acid transfer methods that disable DNA repair in cancer cells: lipid-based nanovectors vs sepiolite,
  - measure of the fluorescence carried by radiosensitising nanoparticles to assess the effectiveness of proton therapy and the dose delivered locally,
  - calibrated biodosimeter for local assessment of the biological effects of medical irradiation,
  - study of the chemoradiotherapeutic efficacy of radiosensitising nanoparticles loaded with active substances in murine models of human cancers,
  - measure of the efficacy of lncRNA antisense oligonucleotides, in combination with MAP kinase inhibitors, to inhibit tumour growth in melanoma and renal cancer CDX and PDX,
  - isolation and in ovo amplification of circulating tumour cells for routine clinical use,
  - high-intensity focused ultrasound surgery with thermometric ultrasound guidance for the treatment of breast tumours,
  - radiofluorinated neurotensin analogues for PET identification of patients eligible for vectored internal radiotherapy,
  - use of stimulated Raman scattering to obtain instant histological data on intraoperative biopsies without labelling or cryosection,
  - antibody-loaded vectors to map and analyse the maturation dynamics of invadopodia in primary or metastatic melanoma cells;
- compounds or vectors development for therapeutic purposes:
  - effects of an anti-EG-VEGF antibody in the treatment of choriocarcinoma and characterisation of its interaction with methotrexate,
  - smart molecular systems releasing calcium channel inhibitors into the tumour microenvironment to eradicate glioblastoma stem cells,
  - calcium phosphate cement loaded with nanoparticles for local release of active principles in osteosarcomas,
  - prohibitin inhibitors with antiproliferative activity in osteosarcoma,
  - hybrid inhibitors of DNMT/EZH2 epigenetic factors to fight chemoresistance in multiple myeloma,
  - inhibitors of the UBE2N protein to sensitise organoids derived from ovarian cancer to PARP inhibitors,
  - nanovector releasing into mitochondria an inhibitor of the formation of the AIF/CHCHD4 complex involved in cell survival,
  - submicronic vectors carrying T or NK cell ‘engagers’ (bispecific anti-tumour and antiCD3 or CD16 antibodies),
  - active and selective compounds targeting p53 mutants and their partners in gastric cancer,
  - compounds inhibiting UBASH3B protein, a negative regulator of the mitotic spindle assembly checkpoint,
  - inhibitors of STARD3 cholesterol transfer protein specifically involved in tumour cell growth.

FIGURE 4
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PCSI PROGRAMME IN 2022 ACCORDING TO THE CSO CLASSIFICATION



Workshop on French radiobiology research field

In July 2022, ITMO Cancer-Aviesan organised a workshop to reflect on the state of the French radiobiology research field. On that occasion, the ITMO and its committee of experts received scientists from various parts of the research community in this field (research organisations/ institutes, networks, learned societies, etc.): CNRS (GDR MI2B – Modelling in instrumentation for medical imaging, IN2P3, INSB), Institut Curie, Inserm, CEA, IRSN, RadioTransNet and ResPlaNDIR networks. They came to present the status of their structure around the following topics:

- main lines and priorities of the radiobiology research field;
- assessment of strengths, weaknesses, and main obstacles;
- elements of medium- and long-term prospects.

The findings and avenues for action considered during this workshop will lead to the drafting of a manifesto intended for supervisory authorities and ministries, which will list the challenges and major projects for the next 5-10 years and the needs and limitations that have to be explored. Working groups are being set up to continue the reflection process.

INTERDISCIPLINARY APPROACHES IN ONCOGENIC PROCESSES AND THERAPEUTIC PERSPECTIVES: MATHEMATICS AND COMPUTER SCIENCE CONTRIBUTION TO ONCOLOGY MIC PROGRAMME

Initiated in 2019 following the redesign and split of the previous PMSI programme (physics, mathematics and engineering sciences related to cancer), the MIC programme (mathematics and computer science contribution to oncology programme) aims to improve understanding of cancer diseases and improve patients' prognosis, thanks to contributions from mathematics and computer science. Indeed, recent technological revolutions have progressively placed these disciplines at the centre of large-scale studies, which have become crucial for oncology research. The programme is intended to unlock conceptual and methodological barriers at the frontier of mathematics, computer science and oncology.

TABLE 4
FEATURES OF THE MIC PROGRAMME IN 2022

Objectives	To improve understanding of cancer diseases and improve patients' prognosis thanks to contributions from mathematics and computer science
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€3.0M**
Proposals submitted	19
Projects selected	8
Selection rate	42%

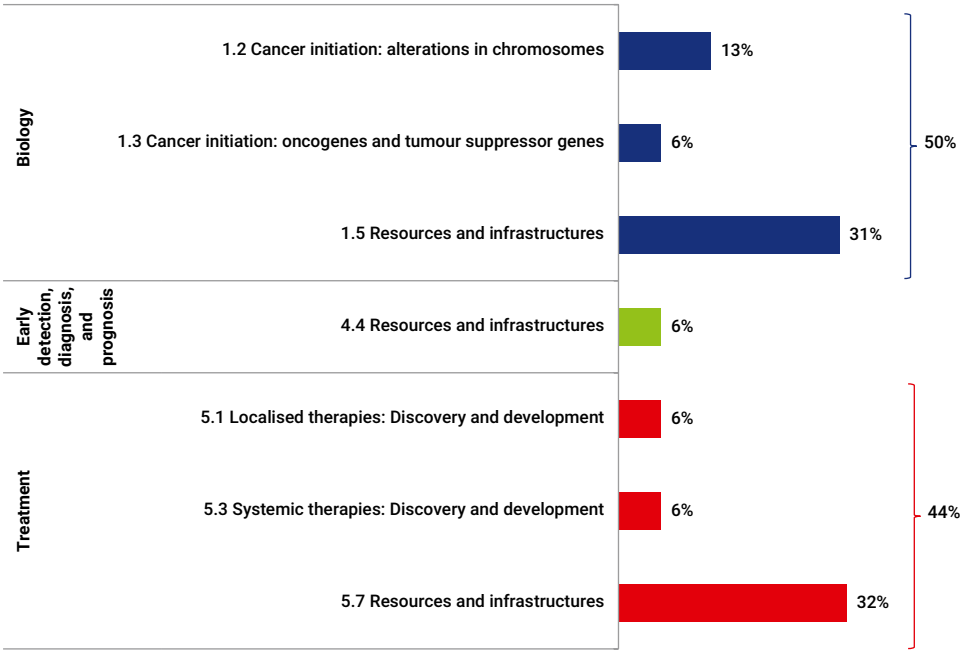
2022:
8
projects selected
for a total amount of
€3.0M

Projects funded in 2022 focused on the analysis and modelling of available big data multiomics (genome, transcriptome, miRNome, (phospho)proteome) or histological data obtained on tumour (including single cell) or healthy tissues. The projects concerned several types of cancer (glioblastoma, osteosarcoma, adrenocortical carcinoma, ENT cancers, medulloblastoma, myeloproliferative neoplasm) and aimed to improve the understanding of the molecular mechanisms of cancer, optimise existing treatments, identify new therapeutic targets, or predict disease outcomes.

Webinars to promote the MIC 2023 call for proposals

On the occasion of the launch of the MIC 2023 call for proposals, ITMO Cancer-Aviesan and the Cancer Unit of Inserm's Department of Programme Assessment and Follow-up organised a series of webinars in December 2022 to present the programme to the mathematical and computer science communities interested in cancer research. Context, objectives, eligible disciplinary fields and regulatory issues were detailed, with a particular focus on the nature and quality of the data used to develop new methodologies, as well as the need to validate these innovative methodologies in real-life conditions. Part of these webinars involved a Q&A session with the audience.

FIGURE 5
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE MIC PROGRAMME IN 2022 ACCORDING TO THE CSO CLASSIFICATION



Comparative study of PMSI, PCSI and MIC programme features

In order to place more emphasis on chemistry, mathematics and computer science, the PMSI programme was split into two programmes – PCSI and MIC – in 2019. At the end of 4 years of programming these new calls for proposals (2019-2022), an analysis was conducted to determine whether the objectives of the PMSI redesign had been achieved. The main conclusions are as follows:

- medicinal chemistry, as well as mathematical and computational approaches applied to oncology, have taken up a more important role with the creation of PCSI and MIC;
- physics-centred approaches remained well represented in parallel with the funding of these new topics given the increase of the total budget amount;
- new communities entered the competition: there is only partial overlap between the communities submitting proposals to PCSI or MIC and those submitting proposals to PMSI, and the scientists who have submitted proposals to PCSI or MIC had little or no experience in cancer research.

SUPPORT FOR CANCER RESEARCH EQUIPMENT

The "Equipment" programme was launched in 2016, in line with the 3rd Cancer Control Plan and a recommendation from the INCa Scientific advisory board. It is aimed at supporting equipment acquisition to foster the development of ambitious research in the field of oncology, to encourage interactions between research teams, and to increase the attractiveness and the position of French teams on the international arena.

TABLE 5
FEATURES OF THE EQUIPMENT PROGRAMME IN 2022

Objectives	To foster the development of ambitious research in the field of oncology, to encourage interactions between research teams, and to increase the attractiveness and the position of French teams on the international arena.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€4.2M**
Proposals submitted	52
Projects selected	**24**
Selection rate	46%

Devices funded in 2022 were mainly intended for imaging (50%), cellular characterisation and histology (33%) and animal model studies (13%). They will be used to monitor cell behaviour in real time, characterise extracellular vesicles, explore tumour and microenvironment heterogeneity (transcriptome, proteome, metabolome) at the single-cell level, visualise the spatial organisation of tumour, microenvironment and immune cells, study telomeres and chromatin structure, search for epigenetic markers, carry out non-invasive longitudinal monitoring of mouse models, etc.

ITMO Cancer-Aviesan and the European UNCAN initiative

The initiative to UNderstand CANcer is one of the 13 specific objectives of the Mission on Cancer and one of the ten flagships of Europe's Cancer Beating Plan. The Coordination and Support Action (CSA) "4.UNCAN.eu" is planned to generate a blueprint for UNCAN.eu by 2023. ITMO Cancer-Aviesan was involved in the very first steps of UNCAN.eu by participating in:

- Setting-up the French task force who applied for the coordination of 4.UNCAN.eu CSA and was selected in 2022;
- Launching the UNCAN.eu initiative at the "Joining European forces to understand cancer" meeting organised in Paris during the French Presidency of the European Union (June 23rd 2022).

FIGURE 6
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE EQUIPMENT PROGRAMME IN 2022 ACCORDING TO THE CSO CLASSIFICATION

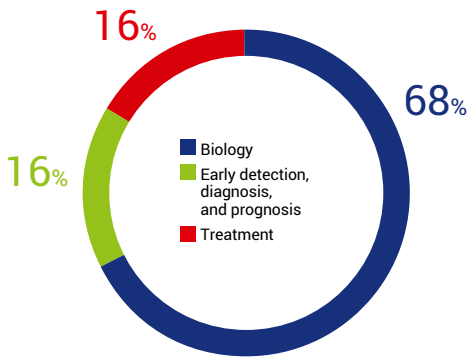
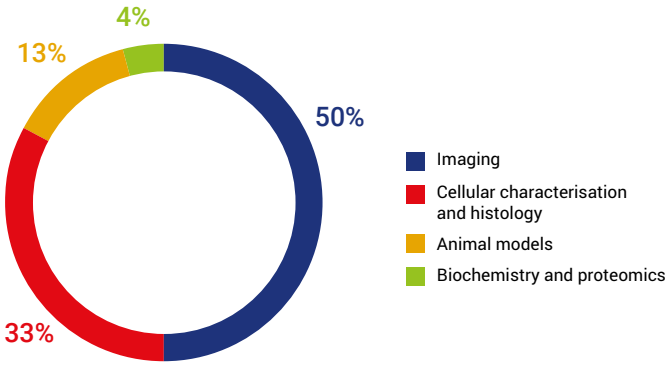


FIGURE 7
CATEGORIES OF FUNDED PROJECTS IN THE EQUIPMENT PROGRAMME IN 2022



FPEU High-Level Conference on Citizen Engagement in European Missions: the Cancer Europe Mission workshop

On the 21st of March 2022, the French Ministry of Higher Education, Research and Innovation organised a high-level conference of the French Presidency of the European Union on citizen engagement in the 5 Horizon Europe Missions. For that event, the Cancer Europe Mission held a workshop, with the objective of defining the necessary framework to facilitate the involvement of citizens in the future actions of the Cancer Mission at European and Member State levels. In close collaboration with the vice-chair of the Mission's board, ITMO Cancer-Aviesan contributed to the organisation of the workshop by suggesting some topics and potential speakers.

Canceropole evaluation

In anticipation of the next wave of canceropole designations, which will cover the 2023-2027 period, the Institute wished to have these structures reviewed by a committee composed of independent external experts in 2022. This review was an opportunity to make a comprehensive assessment of canceropoles' actions in the service of the cancer research community, but also to identify areas for improvement.

This evaluation was carried out in 2 steps:

- ***1st step: review of the 2018-2022 designation (April 2022)***

On the basis of written activity reports, including a detailed self-assessment, and hearings with the coordination teams of the 7 canceropoles, the evaluation committee (EC) carried out an initial assessment of the achievements and actions of the canceropoles with regard to missions, objectives and monitoring indicators planned in their 2018-2022 Objectives and Performance Contracts (COP).

In this overview, the EC once again recognised the added value of these structures in the cancer research landscape. In general, the 4 missions[2] defined by the Institute have been taken in hand by all the canceropoles, which have been able to adapt an offering in line with the needs and dynamics of their respective territories. Indeed, most canceropoles have set up an effective system to account for the needs of the scientific community to define their strategy (bottom-up approach).

The external EC having concluded that the 4 missions were still relevant and still met a need within the cancer research community, these missions will therefore be renewed in the same way for the next term. In addition, and with the aim of continuous efficiency and quality improvement, this new designation phase will pay particular attention to 2 complementary objectives:

- strengthening of collaborations between canceropoles and exchanges of expertise, in order to highlight the actions which have been successful in some canceropoles, and identify the possibility of generalising them to others. In addition, new inter-canceropole projects are being encouraged during this new designation: they will strengthen ties between canceropoles and sharing of resources. These collaborations could be set up based on strengths, regional expertise and common interests, in particular in relation to niche themes for which the critical mass of researchers is insufficient at a single-region or inter-region scale;
- strengthening of actions promoting health democracy, through active and recognised integration of patients within canceropole governance bodies, in call for proposals selection committees led by canceropoles, in working groups, etc.

2. Reminder of the canceropoles' 4 missions:
• To integrate cancer research into a regional or inter-regional dynamic based on knowledge of the regional ecosystem (research, health, industry, politics);
• To facilitate collaborations between Canceropole researchers (within the same discipline or in a multidisciplinary approach);
• To support researchers (assisting emerging projects, in the development of national and international projects, supporting the mobility of young researchers, etc.);
• To foster innovation detection and subsequent technology transfer.

- ***2nd step: proposal of new action plans for the 2023-2027 designation (October 2022)***

In line with the actions carried out within the 2018-2022 COP framework, the canceropoles have therefore proposed new action programmes for the next 5 years. These actions were presented to the EC through written applications and oral presentations. The committee assessed the relevance and feasibility of the proposed programmes, as well as recommendations for their implementation.

Several aspects were favourably viewed and highlighted by the EC:

- the important work carried out by canceropoles accounting for the critiques and recommendations issued during the 1st step of the evaluation, in particular concerning identified strengths and weaknesses. The canceropoles have presented an adapted and adjusted action plan, with the aim of filling certain gaps;
- the quality/relevance of the objectives and actions presentation. There is a constant drive to improve coordination and integrate multidisciplinarity in all canceropoles;
- the benefits of structuring research networks, showing interesting results and allowing effective pooling of resources and skills;
- the identification and promotion of original ideas such as the integration of social and territorial inequalities as research fields/themes;
- the progressive development of synergistic inter-canceropole collaborations. Several inter-canceropole working groups are being set up, as recommended by the committee;
- the accuracy and relevance of the approach initiated to promote health democracy.

Support for paediatric cancer research

Thanks to the renewed allocation of €5M by the French Minister for Higher Education, Research, and Innovation, 2 calls for proposals were launched in 2022.

SUPPORT FOR "HIGH-RISK – HIGH-GAIN" PAEDIATRIC CANCER RESEARCH PROJECTS

This call for proposals, which has been launched for the third consecutive time since the year 2020, aims to support highly innovative research projects that will open up new and original avenues and produce concrete advances in paediatric oncology.

The aim is to fund original and audacious research projects that are conceptually new and risky, considered as "High Risk-High Gain", which would not be eligible for funding in the context of traditionally existing calls for proposals.

These projects must be based on significant conceptual risk-taking, in order to propose a new or even disruptive approach. The potential impact of the proposed projects on paediatric oncology cancer research must be of a high level.

In 2022, 6 out of a total of 19 projects were selected for funding, for an overall budget of € 3,250,211 (Table 6).

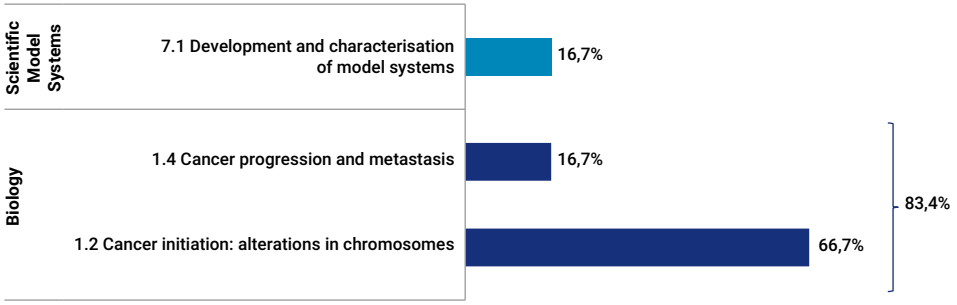
TABLE 6
FEATURES OF THE "HIGH-RISK – HIGH-GAIN" PAEDIATRIC CANCER RESEARCH PROJECTS PROGRAMME IN 2022

Objectives	Enable the development of conceptually new and risky projects which would be ineligible for funding in the context of traditionally existing calls for proposals.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€3.25M**
Proposals submitted	**19**
Projects selected	**6**
Selection rate	**31.6%**

The selected and funded projects are aimed at:

- developing a proof-of-concept of controlling the developmental hierarchy of paediatric tumours via inhibition of microRNA modules;
- using gene edition as targeted therapy in the treatment of hepatoblastoma;
- deciphering cisplatin mutational signature in hepatoblastoma for early detection of chemoresistance and new treatment;
- studying newly identified neogenes in chimeric oncogenic transcription factor-driven tumours of children as targets for immunotherapy;
- studying epiclones and resistance to epidrugs in rhabdoid tumours;
- investigating autoantibodies neutralizing immune responses as a novel factor of paediatric lymphomas associated with Epstein Barr virus infection.

FIGURE 8
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION OF THE "HIGH-RISK-HIGH GAIN" PAEDIATRIC CANCER RESEARCH PROGRAMME



The CSO typology of projects funded shows that the projects are mainly focused on basic research on cancer biology and model development.

INNOVATIVE MODELS IN PAEDIATRIC ONCOLOGY

The aim of this call for proposals is to extend our knowledge in paediatric oncology, in particular on the causes of paediatric cancers, on cellular mechanisms of tumour progression, on tumoral microenvironment, and on how paediatric cancers escape the immune system, through research projects based on innovative models. The proposed models and modelling approaches may either:

- already exist, the use of which will be new in the field of paediatric oncology (possible modifications and/or optimisation of the original model). Their relevance and adaptation to paediatric cancers must be justified with regard to the specificity of these cancers;
- or be developed within the framework of the project. The validity of these newly developed models must be demonstrated and the applications of these models must be defined and tested within the project.

In addition, all the proposed projects must focus on relevant issues relating to paediatric cancers (e.g.: methodological barriers clearly identified by the scientific community or pathologies for which the lack of a model is established).

In 2022, 3 applications out of a total of 7 were selected for funding, for an overall budget of € 2,362,173 (Table 7).

TABLE 7
FEATURES OF THE INNOVATIVE MODELS IN PAEDIATRIC ONCOLOGY PROGRAMME IN 2022

Objectives	Provide new knowledge in paediatric oncology through research projects based on innovative models
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€2.36M**
Application submitted	**7**
Application selected	**3**
Selection rate	**42.9%**

The selected and funded projects are aimed at:

- characterising a unique collection of immune-organoid models derived from rhabdomyosarcoma patient samples and performing high-throughput drug screens while developing mathematical models to design innovative therapeutic combinations;
- modelling the developmental dynamics of the bone marrow microenvironment for studying neuroblastoma dissemination and risks of secondary acute myeloid leukaemia;
- modelling ETO2-GLIS2 paediatric acute megakaryoblastic leukaemia transformation trajectories using human hematopoietic cells to identify therapeutically-actionable vulnerabilities.

The CSO typology of funded projects shows that the projects are exclusively focused on basic research in model development.

French Presidency of the Council of the European Union

Summary with paediatric focus/conclusions

The first edition of the European Meetings of the French National Cancer Institute took place in a new format, within the framework of the French Presidency of the Council of the European Union, on the occasion of World Cancer Day, on 3 and 4 February, 2022.

The aim of these meetings was to intensify cooperation and joint action in order to further advance the fight against cancer for the benefit of the populations of the 27 Member States of the European Union.

At the end of 2021, the French National Cancer Institute undertook to organise numerous exchanges with the support of 150 international experts in 5 workshops with the aim of accelerating efforts to fight cancer at the European level.

The joint political declaration, unveiled at the end of these workshops, represented a strong commitment by the trio holding the Presidency of the Council of the European Union in 2022 and 2023, composed of the French Minister of Health, Olivier Véran, and his Swedish and Czech counterparts, Lena Hallengren, and Vlastimil Válek.

Cancer will become the leading cause of death in the world in the next decade, and the number of cancer deaths in the EU is expected to increase by more than 24% by 2035. With this political declaration, the trio reaffirmed the political, scientific and operational prioritisation of the fight against cancers, particularly paediatric cancers, in the European Union. With regard to the fight against childhood cancers, the political declaration calls for the revised European regulation on medicinal products for paediatric use to enter into force as quickly as possible. More broadly, it calls on all public and private sector stakeholders to commit to the establishment of European clinical trials on paediatric cancers and to sharing follow-up data on a European scale.

In addition, the political declaration includes the 32 new concrete actions proposed by the experts around 5 priority themes:

- 1. poor prognosis cancers;
- 2. cancer prevention;
- 3. cancer and employment;
- 4. paediatric cancers;
- 5. international cooperation in the fight against cancer.

The actions concerning paediatrics are grouped around 4 focus:

FOCUS 1. ACCELERATE AND DEVELOP CLINICAL RESEARCH:

Action 1: Ensure that the regulatory processes of the EU Regulation on paediatric and orphan medicines are addressed separately. Define concrete actions to speed up the implementation of the Paediatric Regulation in its revised version and foster innovation.

The revision of the paediatric regulation is expected in 2023 and should:

- Encourage research and development of medicines for children;
- Contribute to guaranteeing availability of and timely access to paediatric medicines;
- Make sure that legislation is adapted to technological and scientific progress;
- Provide efficient and productive procedures for the assessment and authorisation of orphan and paediatric medicines.

Action 2: Establish the possibility at a European level for all children and young adults to access clinical trials, for all relevant therapeutic regimens.
Access to clinical trials is heterogeneous between European countries and generates inequalities.
There is a need to:

- Facilitate access to paediatric clinical trials and strengthen the infrastructures for conducting clinical trials in all European countries;
- Enable all children and young adults with cancer to have access to existing clinical trials, wherever they live and wherever the clinical trial takes place.

Action 3: Fund the development of clinical research through European grants.
In paediatric oncology, continued progress is dependent on European coordination in research, especially for clinical trials, where the ability to recruit from multiple countries facilitates the implementation of those trials, improves their quality and opens them for all children. Adequate and coordinated funding is needed for these trials.

Funding clinical research through European grants can allow each country to benefit simultaneously from the necessary funding to run clinical trials.

FOCUS 2. REINFORCE COHORTS

Action 4: Coordinate childhood and young adult cancer follow-up cohorts (particularly on long-term follow-up, management of sequelae) at a European level.
Collection of long-term data from cancer survivors allows long-term adverse effects following cancer treatment to be evaluated. It also represents a chance to improve the support given to cancer survivors, long-term monitoring and follow-up care, and management of sequelae.

FOCUS 3. DEVELOP, CONSOLIDATE AND SHARE DATA

Action 5: Establish a common database at a European level (European Health Data Space) and specify the types of data.
Through enhanced data sharing, we can improve our understanding of cancer biology to improve preventive measures, diagnosis, treatment, quality of life, and survivorship. However, information on diagnosis, treatment, and outcomes is often stored at the hospital or institution where a child is treated. Difficulties sharing this data hinder scientific research in childhood cancer.

FOCUS 4. ACCELERATE THE STRENGTHENING OF CURRENT EUROPEAN STRUCTURES

Action 6: Ensure the integration of paediatric cancers as a priority in EU Member States' national strategies in the fight against cancer.
Paediatric cancers should be considered a priority in all EU Member States' national cancer strategies.

Action 7: Reinforce the European Paediatric Cancer Reference Network.
The European Paediatric Cancer Reference Network (ERN PaedCan) was established to reduce inequalities in survival of children with cancer by providing high-quality cross-border healthcare, accessible wherever the children live. This European Union initiative plays a key role in the fight against paediatric cancers.

Action 8: Ensure coordination between paediatric infrastructures and the future European network of Comprehensive Cancer Centres.
The European Network of Comprehensive Cancer Centres, a flagship initiative of Europe's Beating Cancer Plan, is an opportunity to improve access to quality diagnosis, treatment, research and care across Europe.

Action 9: Establish new ways to coordinate and follow actions specifically related to paediatric cancers.

The details of the proposals of the dedicated working group can be found on the following link:

https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Retour-sur-les-Rencontres-europeennes-2022

Support for professional careers in cancer research

SUPPORT FOR THE ATIP-AVENIR PROGRAMME

Under a partnership between CNRS and Inserm, the aim of the ATIP-Avenir programme is to enable young scientists to create and lead their own research team within an established Inserm or CNRS laboratory in France. ITMO Cancer-Aviesan contributes to the funding of the awardees pursuing a cancer research project.

TABLE 8
FEATURES OF THE ATIP-AVENIR PROGRAMME IN CANCER RESEARCH IN 2022

Objectives	To promote the establishment of promising young Principal Investigators (PI) in cancer research by funding their starting team for 3 years and/or for a 2-year extension
Programming institution	CNRS and Inserm
Operating institution	CNRS and Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€780,000**
Projects funded	**2 new projects & 3 extensions**

The 2 new projects funded in 2022 are aimed at: characterising the chromatin network that stabilises and repairs replication fork damages, in order to identify new chromatin targets to overcome chemoresistance; deciphering how glioblastoma (GBM) heterogeneity affects the metabolic determinants of GBM patient-derived stem cells adaptation to stress.

SUPPORT FOR THE ANR JCJC PROGRAMME

The JCJC (Jeunes chercheurs ou jeunes chercheuses) programme is one of the four funding instruments of the annual Generic Call for Proposals of the French National Research Agency (ANR). It is designed to give young researchers in various scientific fields access to co-funding in a large number of research themes, basic or applied, in addition to their allocated recurrent funding. In 2020, ITMO Cancer-Aviesan developed a partnership with ANR to fund JCJC projects related to cancer research.

TABLE 9
FEATURES OF THE JCJC PROGRAMME IN CANCER RESEARCH IN 2022

Objectives	To support established young researchers with additional funding of their project in the cancer research field.
Programming institution	French National Research Agency (ANR)
Operating institution	French National Research Agency (ANR)
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€670,000**
Projects funded	2

The 2 projects funded in 2022 are aimed at exploring: granulopoiesis alteration linked with chronic inflammation contexture in lung cancer; involvement of arginine methyltransferase PRMT5 in glucocorticoid-induced resistance to chemotherapy in triple-negative breast cancer.

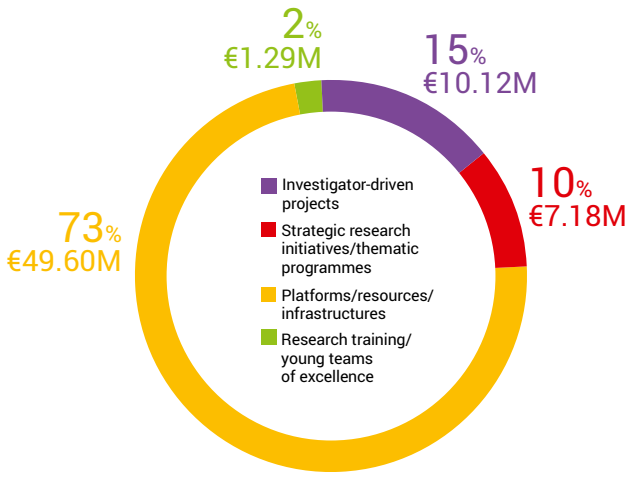
TRANSLATIONAL AND INTEGRATED CANCER RESEARCH

Translational research in oncology aims to bridge the gap between basic research and clinical research in order to translate scientific progress into products and procedures that benefit patients.

In line with the previous Cancer control plans, translational research receives significant support through dedicated calls for proposals, programmes to strengthen training in this research field and a policy of designated multidisciplinary integrated research sites.

In 2022, support for translational and integrated cancer research amounted to:

€68.19M



Supporting translational cancer research

NATIONAL TRANSLATIONAL CANCER RESEARCH PROGRAMME PRT-K

The objective of the PRT-K (National translational cancer research programme) call for proposals, launched for the first time in 2007 and recurrent since 2009 in partnership with DGOS, a directorate of the French Ministry of Health, is to promote interdisciplinary projects, bringing together laboratory researchers and clinicians. Sharing of specific expertise, skills and knowledge should promote the translation of scientific and medical discoveries into clinical advances for cancer patients.

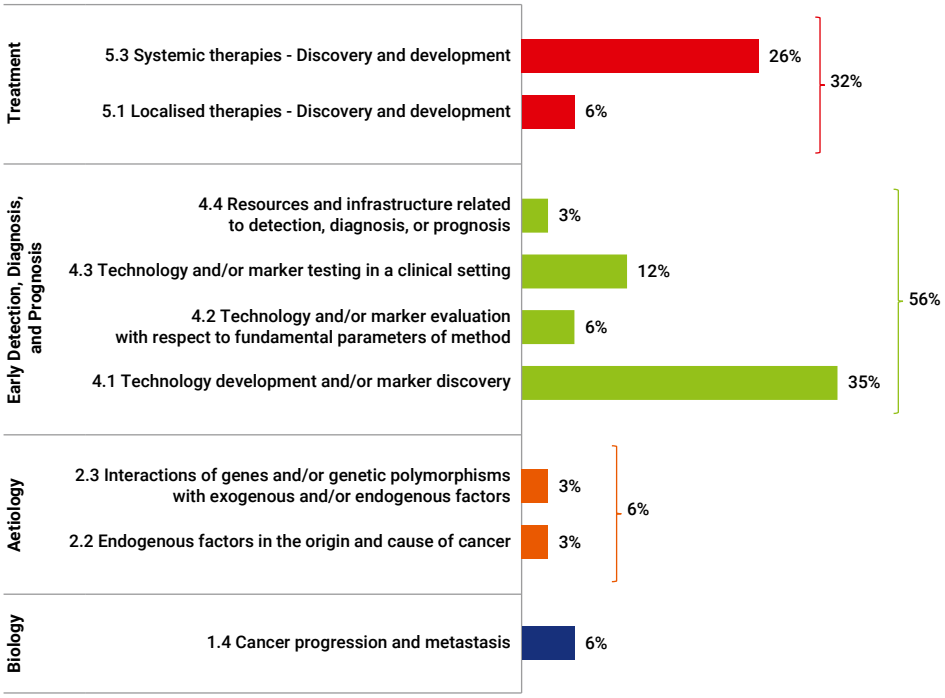
In 2022, 17 projects were selected for funding, out of the 128 submitted, representing an overall budget of €10.14M (€7.12M INCa + €3.02M DGOS) (Table 10).

TABLE 10
FEATURES OF THE PRT-K PROGRAMME IN 2022

Objectives	To accelerate the transfer of knowledge with a view to its prompt application in clinical practice for the benefit of patients, by giving researchers an incentive to develop multidisciplinary projects in close collaboration with clinicians, in order to improve prevention, early detection, diagnosis, treatment, and comprehensive care of cancer patients.
Programming institution	INCa/Ministry of Health (DGOS)
Operating institution	INCa
Funding institution	INCa/Ministry of Health (DGOS)
Funding	**Total: €10.14M** **INCa: €7.12M** **DGOS: €3.02M**
Proposals submitted	**128**
Projects selected	**17**
Selection rate	**13%**

In keeping with the programme objectives, and previous years, almost 60% of the projects selected in 2022 are studying early detection, diagnosis, and prognosis, in particular discovery or identification and characterisation of biomarkers. About a third of projects are focusing on the development of treatments, especially discovery and development of systemic therapies (Figure 9).

FIGURE 9
DISTRIBUTION OF PROJECTS SELECTED IN 2022 ACCORDING TO THE CSO CLASSIFICATION



EUROPEAN TRANSLATIONAL CANCER RESEARCH PROGRAMME (TRANSCAN)

The TRANSCAN-3 network, preceded by TRANSCAN-1 and TRANSCAN-2, is a cross-national cooperation, bringing together 31 funding organisations from 20 countries, with the common goal of supporting high-impact translational cancer research through joint transnational calls for proposals, and through efficient investment of dedicated national/regional public funding, leveraged with foundation/charity-based resources and EU financial support.

In April 2021, TRANSCAN-3 launched its first Joint Transnational Call for research proposals (JTC-2021) co-funded by the European Commission on "Next generation cancer immunotherapy: targeting the tumour microenvironment". The projects were selected in May 2022.

TABLE 11
FEATURES OF THE TRANSCAN PROGRAMME IN 2022

Objectives	To develop innovative transnational projects in translational research on next-generation cancer immunotherapy (targeting the tumour microenvironment).	
Programming institution	TRANSCAN-3	
Operating institution	28 organisations/19 countries	
Funding institution	All funding organisations	France
Funding	**€26M**	**Total: €4.6M** **INCa: €3.2M** **ARC Foundation: €1.3M**
Proposals submitted	**161**	83 French research teams. 13 Letter of intent with French coordination.
Projects selected	**20**	**18 French teams in 13 projects.** **1 project with French coordination.**
Selection rate	**12%**	

This call led to the funding of 20 projects out of the 161 proposals submitted. INCa has supported 13 French teams participating in 10 projects, out of the 18 French teams involved in 13 selected projects (the 5 other teams are funded by the ARC Foundation).

The total amount of French funding is €4.6M, including €3.2M from INCa and €1.3M from the ARC Foundation for Cancer Research (ARC Foundation). Table 11 presents the main features and the results of this call for proposals.

Half of the funded projects are focusing on the discovery, development or study of the mechanism of action of systemic treatments (CSO5.3) (Figure 10). The other half of the projects are focusing on the identification and validation of new bio-markers or technology in order to improve early detection, diagnosis, or prognosis of cancers (CSO4).

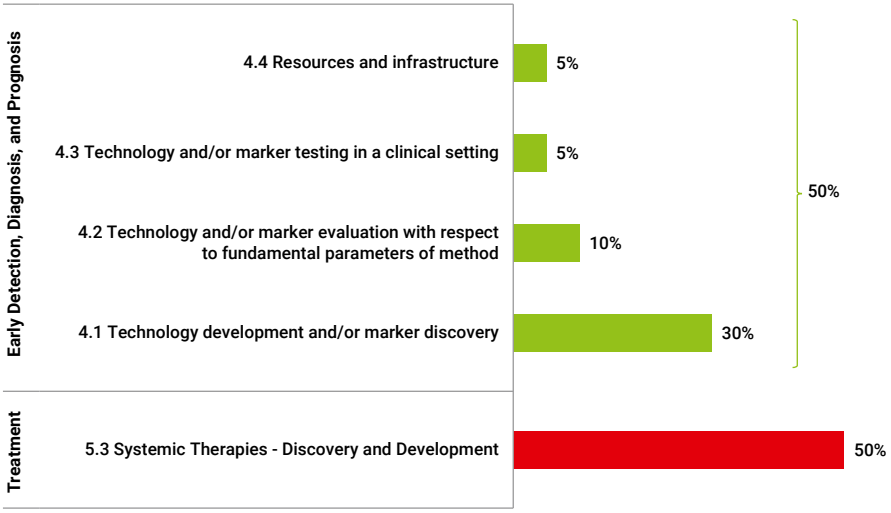
Launch of JTC22: tackling the challenges of hard-to-treat cancers

In May 2022, TRANSCAN-3 launched its second Joint Transnational Call for research proposals (JTC2022) on "Novel translational approaches to tackle the challenges of hard-to-treat cancers from early diagnosis to therapy".

The projects will be selected in mid-2023 and should commence by the end of 2023.

2022:
13
French teams (in 10 projects) funded by INCa for a total amount of
€3.2M

FIGURE 10
DISTRIBUTION OF THE SELECTED PROJECTS (WITH FRENCH TEAMS FUNDED BY INCA) ACCORDING TO THE CSO CLASSIFICATION



High-risk – high-gain on poor prognosis cancers

Despite the progress made in the treatment of many cancers, some continue to have a poor prognosis because of (1) delayed screening, (2) tumour access difficulties, (3) rapid and aggressive progression, (4) treatment resistance, or (5) lack of specific therapeutic solutions.

Within the framework of the Ten-year cancer control strategy, France has set an objective of improving the survival rate of these cancers significantly by 2030.

The incidence of some of these cancers continues to be on the rise. Much greater effort must therefore be devoted in order to ensure significant improvements in survival rates for this type of cancer.

In order to encourage novel approaches and support proposals liable to generate disruptive innovations, the French National Cancer Institute has set up new "High-Risk – High-Gain" (HR/HG) type calls for proposals (CFPs) (published in November 2021).

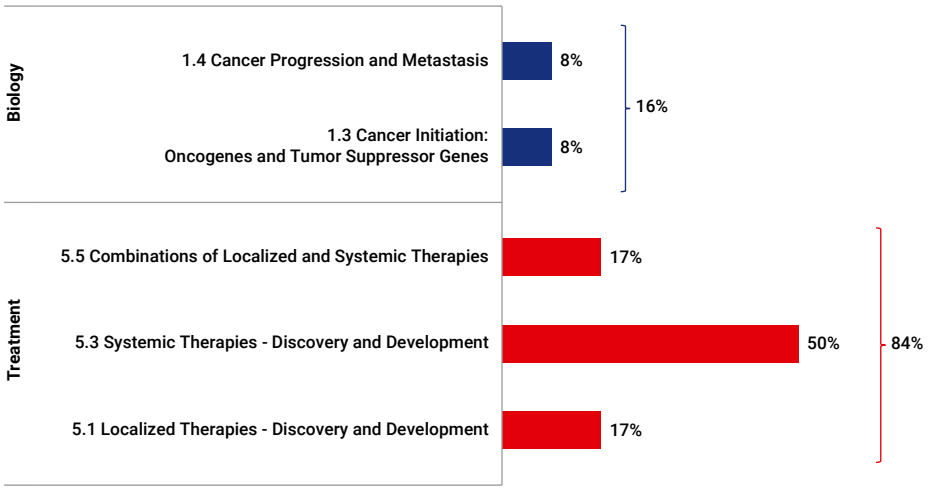
Six out of a total of 32 projects were selected for funding in March 2022, for an overall budget of €3.615M.

TABLE 12
FEATURES OF THE "HIGH-RISK – HIGH-GAIN" POOR PROGNOSIS CANCERS RESEARCH PROJECTS PROGRAMME IN 2022

Objectives	To accelerate the generation of new scientific knowledge through greater risk-taking in research, leading to revolutionary innovations which will help meet challenges (in terms of early screening or diagnosis, improving knowledge on the mechanisms of onset of these cancers or of treatment escape, developing new treatments, etc.) raised by these cancers with poor prognosis.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€3.615M**
Proposals submitted	**32**
Projects selected	**6**
Selection rate	**19%**

Of the 6 projects selected for funding, two are focusing on glioblastoma, two on acute myeloid leukaemia, one on hard-to-reach solid tumours, and one on a non-site-specific cancer. The distribution of the selected projects according to the CSO classification shows that most projects relate to treatment area of investigation (83%).

FIGURE 11
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION



Four projects are aimed at developing new therapeutic strategies:
- in response to the constraints associated with crossing the blood-brain barrier: internal vectorised radiotherapy with focused ultrasound;
- antitumour immunotherapy triggered by cold plasma;
- systemic administration of an immunostimulant to stimulate the innate immune system;
- transforming a shamanic ritual (known as Kambo) into an effective therapy.

The two other projects are focusing on understanding the mechanisms that contribute to resistance to treatment, in order to understand:
- how senescent endothelial cells promote genomic instability and increase the aggressiveness of recurrent glioblastoma;
- the link between TP53 mutations and resistance mechanisms, control of iron metabolism during metabolic and therapeutic stress.

Multi-thematic and multi-disciplinary research: reducing radiation therapy side-effects and improving quality of life

This programme was conducted within the framework of the Ten-year cancer control strategy launched in February 2021. It is part of FOCUS 2: Reducing sequalae and improving quality of life.

The scope of this call is:
- to support projects aimed at enhancing knowledge and the means to reduce side-effects caused by radiotherapy;
- to promote a cross-cutting multidisciplinary approach covering different research disciplines (basic research, translational research, clinical research, research in human and social sciences) and fields (medical oncology, radiation therapy, radiobiology, medical physics, imaging, dosimetry, etc.).

Out of 38 submitted proposals, 4 projects were selected for funding, representing a total amount of €3.83M (Table 13 and Figure 12).

TABLE 13

FEATURES OF THE MULTI-THEMATIC AND MULTI-DISCIPLINARY RESEARCH: REDUCING RADIATION THERAPY SIDE-EFFECTS AND IMPROVING QUALITY OF LIFE PROGRAMME IN 2022

Objectives	To reduce radiation therapy side-effects and improve quality of life
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€3.83M**
Proposals submitted	**38**
Projects selected	**4**
Selection rate	**10.5%**

2022:

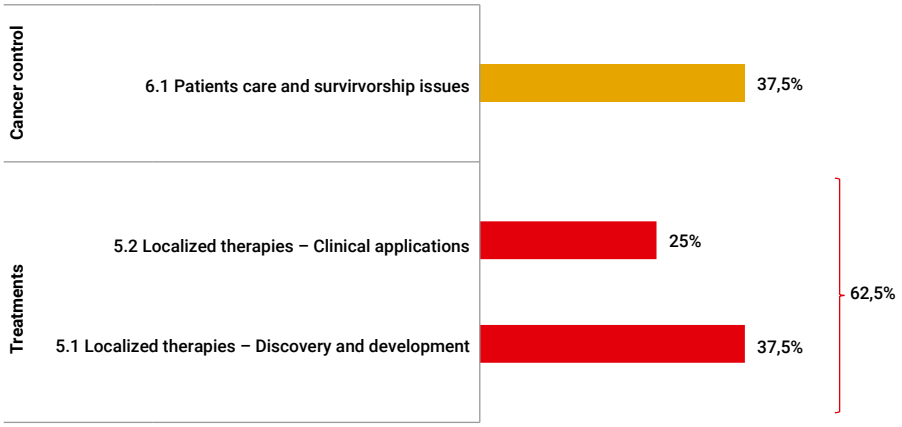
38

proposals submitted; 4 projects selected for a total amount of

€3.83M

FIGURE 12

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE "MULTI-THEMATIC AND MULTI-DISCIPLINARY RESEARCH: REDUCING RADIATION THERAPY SIDE-EFFECTS AND IMPROVING QUALITY OF LIFE" PROGRAMME



Supporting cancer research structuring

SIRIC DESIGNATION

In 2011, the French National Cancer Institute set up a competitive integrated cancer research site (SIRIC) designation strategy, which was continued with a second designation round in 2018. The aim of these programmes was to provide translational cancer research with new operational conditions, with a view to optimising and ramping up the generation of new knowledge, and promoting the dissemination and application of this knowledge in cancer care. The SIRIC designation programme has thus enabled hospital sites to pool their medical, scientific and technological strengths to set up ambitious integrated research programmes in order to fight cancer. These sites included one or more healthcare facilities university hospitals (CHUs) and/or non-profit private hospitals earmarked for cancer care (CLCCs)), research teams (INSERM, CNRS, Universities, INRIA, Engineering schools, etc.) in a range of disciplines (biological sciences and human and social sciences, but also physics, chemistry, computer science, etc).

The importance and priority of this flagship programme was once again underpinned in 2022 with the launch of a third designation phase by the French National Cancer Institute, in partnership with Ministry of Health (DGOS) and Inserm on behalf of ITMO Cancer-Aviesan. This designation maintains the objectives previously defined and which have demonstrated their relevance, i.e.:

- implement a three-fold integration, structuring and development role in order to conduct excellence-based research that can be transferred for the benefit of the general population and those affected by cancer;
- strengthen the level of creativity and international competitiveness of the research projects conducted by their teams on cancer prevention, diagnosis and treatment.

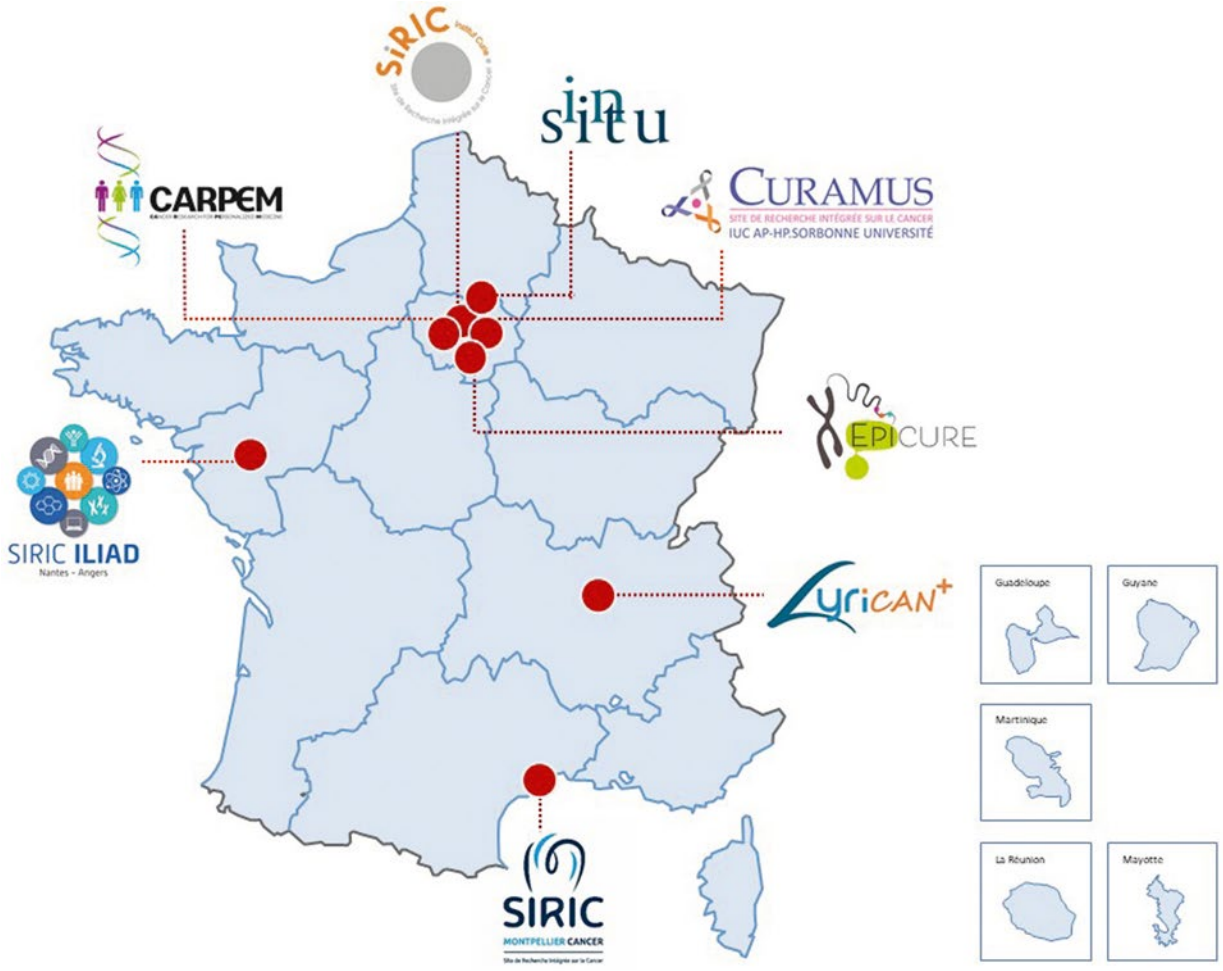
The call for applications was open both to previously designated SIRICs (in 2011, 2012 or 2018) and to new applicants.

Following an international scientific evaluation, eight projects out of the fourteen submitted applications were selected for funding:

- **SIRIC CARPEM³** – CAncer Research in multiple dimensions to accelerate PrEcision Medicine (Paris);
- **SIRIC CURAMUS** – Cancer United Research Associating Medicine, University & Society (Paris);
- **SIRIC Curie** (Paris);
- **SIRIC EPICURE** (Villejuif);
- **SIRIC ILIAD** – Imaging and Longitudinal Investigations to Ameliorate Decision making in multiple myeloma and breast cancer (Nantes-Angers);
- **SIRIC InsiTu** – Insights Into Cancer: From Inflammation to Tumour – Prevent, Intercept, Cure (Paris);
- **SIRIC LYriCAN+** – LYon Recherche Innovation contre le CANcer (Lyon);
- **SIRIC Montpellier Cancer** (Montpellier).

Overall SIRIC funding is supported jointly by a grant from the Institute, DGOS and Inserm on behalf of ITMO Cancer-Aviesan. The allocated budget for the SIRIC programme is approx. €49.6M for a five-year designation period (INCa: €20M; DGOS: €21.6M; Inserm: €8M).

FIGURE 13
GEOGRAPHIC DISTRIBUTION OF THE SIRICS DESIGNATED FOR THE 2023-2027 PERIOD



MED-OSIRIS: Ensuring health data interoperability

MED-OSIRIS is a continuation of the OSIRIS project, supported by INCa with €150K since 2021.

The first objective of the MED-OSIRIS project is to ensure maintenance and updating of the initial OSIRIS data model regarding international health terminologies, new data elements or new data concepts. The extension then consists in working in the field of medical imaging with additional experts beyond the initial OSIRIS group members to extend the initial OSIRIS data model with radiomic and radiotherapy data concepts. Finally, the deployment consists of mapping between the OSIRIS common data model and the FHIR standard, a healthcare standard developed to facilitate exchange of electronic health data between different hospital information systems. This part involves the installation of the OSIRIS-FHIR solution in local warehouses at Institut Curie, Centre Léon Bérard, Institut Bergonié and Bordeaux university hospital.

The second objective is to demonstrate, using a pilot case study (OSIRIS LUNG project), the clinical relevance of the OSIRIS conceptual data model to accelerate innovation. The main objective is to better understand the heterogeneity of the response to targeted therapies and to identify predictive factors or biomarkers of treatment response using real-world data (RWD) from patients with lung adenocarcinoma in the context of EGFR mutation or ALK gene translocation. In 2022, the LUNG-OSIRIS use case was also aimed at demonstrating the feasibility of setting up a standardised database containing RWD with the FHIR-OSIRIS model between two cancer centres and one university hospital.

The work on MED-OSIRIS will be completed in March 2023 and will provide technical solutions as well as a technical report, a synopsis of the work achieved by this multidisciplinary team, and valuable feedback for future use cases.

In 2023, INCa will take over the leadership of the OSIRIS project, and this work will be organised according to four strategic areas:

- maintain the OSIRIS conceptual data model particularly with regard to international health standards;
- extend the current OSIRIS data model particularly with regard to RWD extracted from electronic health records and clinical software;
- disseminate the model across the French national territory particularly by facilitating the OSIRIS community through different web interface or computer tools such as GitHub (https://github.com/InstitutNationalduCancer);
- measure the impact of using the OSIRIS model through scientific challenges and technical projects.

BCBS FOR POOR PROGNOSIS CANCERS

Clinical and Biological Databases (BCBs) were first designed to encourage cooperation between different research teams and clinicians to create, around a common disease, clinical and biological databases associated with biological samples, in order to optimise the collection, integration and cross-disciplinary and multi-disciplinary use of information. The main mission of these BCBs is to organise the creation, development and management of a nationwide prospective cohort focused on a specific disease, in order to collect clinical, biological and genomic data to improve our knowledge of this disease, and to study diagnostic methods and therapeutic practices to refine patient care.

Efforts to significantly improve survival from cancers with a poor prognosis (CPP) must be stepped up. This research effort will take the form of structuring initiatives, in particular the designation of cancer research networks, in conjunction with existing structures.

To consolidate this designation (to be organised in 2023), the Institute has launched a call for applications for the six (out of 14) BCBs addressing these cancers with poor prognosis (table 14) in order to prepare them to support "networks of excellence".

TABLE 14
LIST OF BCBS ADDRESSING POOR PROGNOSIS CANCERS

Cancer	Name of BCB
Stomach/oesophagus	FREGAT
Liver/gallbladder and bile ducts	Network CRB Liver
Pleural mesothelioma	MESOBANK
Pancreas	BACAP
Myeloproliferative disorders/Acute myeloid leukaemia	BCB FIMBANK
Central nervous system	BCB Glioblastoma

The objectives of this initiative are to facilitate access to quality data and biological resources for research teams working on these cancers, in particular those in the "network of excellence", and to improve the use and sharing of data on these cancers.

In this context, an evaluation (based on written reports and a hearing with the BCB Director on 6 July 2022) of these six BCBs has been conducted in order to define an Objectives and Performance Contract (OPC) for each for the next 5 years. Each BCB will receive €416,000 over 5 years (overall budget €2.5M).

4 missions were defined in the OPC:
- bringing BCBs into compliance with "Commission nationale de l'informatique et des libertés" (CNIL) "data warehouse" standards;
- bringing into compliance with the OSIRIS dataset;
- definition of "core data" and systematic transmission to the Institute's cancer data platform, in terms of data sharing;
- increasing support for research teams working on poor prognosis cancers, particularly for those involved in the "CMP networks of excellence" to be designated by the Institute.

RADIOTRANSNET 2.0: NATIONAL RADIOTHERAPY PRECLINICAL RESEARCH NETWORK

Established and designated by INCa in 2017 for 3 years, RadioTransNet is the national preclinical research network for radiotherapy coordinated by Philippe Maingon and Vincent Marchesi.

Structuring the field of preclinical research in radiotherapy remains a priority for the further development and success of oncological radiotherapy in France. The French National Cancer Institute is thus keen to pursue this action further, and has decided to launch a second call for applications in order to designate a national network for preclinical radiotherapy research for the 2022-2025 period. This new designation campaign, for a 4-year period and €400,000 of funding from INCa, should help meet the challenges arising from current knowledge and anticipated needs in the coming years, for ever increasing efficacy in the fight against cancer.

TABLE 15
FEATURES OF THE NATIONAL RADIOTHERAPY PRECLINICAL RESEARCH NETWORK

Objectives	• To promote multi and interdisciplinary collaboration and to improve partnerships between various protagonists in radiotherapy research at a national level; • To foster academic capabilities in terms of innovation, design and management of preclinical projects; • To enhance the international visibility and attractiveness of French radiotherapy research, and to further develop European and international collaboration in this field.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€400,000**
Proposals submitted	**1**
Projects selected	**1**
Selection rate	**100%**

During the 1st year of this 2nd designation, the main activities of RadioTransNet 2.0 were to

1. Set up and update an observatory of preclinical research in radiotherapy.
2. Organise a workshop devoted to proton and hadron therapy (November 2022).
3. Set up a one-year scholarship for master students.

Translational and multidisciplinary training programmes

BASIC AND TRANSLATIONAL RESEARCH TRAINING PROGRAMME (FRFT) BY ITMO CANCER-AVIESAN

Launched in 2007, and led by ITMO Cancer-Aviesan since 2011, the aim of the FRFT programme is to support complementary translational and basic research training of graduates of medicine, pharmacy, dentistry and veterinary science through grants for Master's degrees, PhDs, and postdoctoral positions. In 2019, the programme was reviewed with an emphasis on the career paths of M2 and PhD medical awardees: the analysis pointed out that only a few M2 degree awardees were continuing with research activities. In 2021, the scope of the FRFT programme was therefore reassessed to focus on PhD thesis grants (FRFT-Doc).

TABLE 16
FEATURES OF THE BASIC AND TRANSLATIONAL RESEARCH PHD TRAINING PROGRAMME (FRFT-DOC) IN 2022

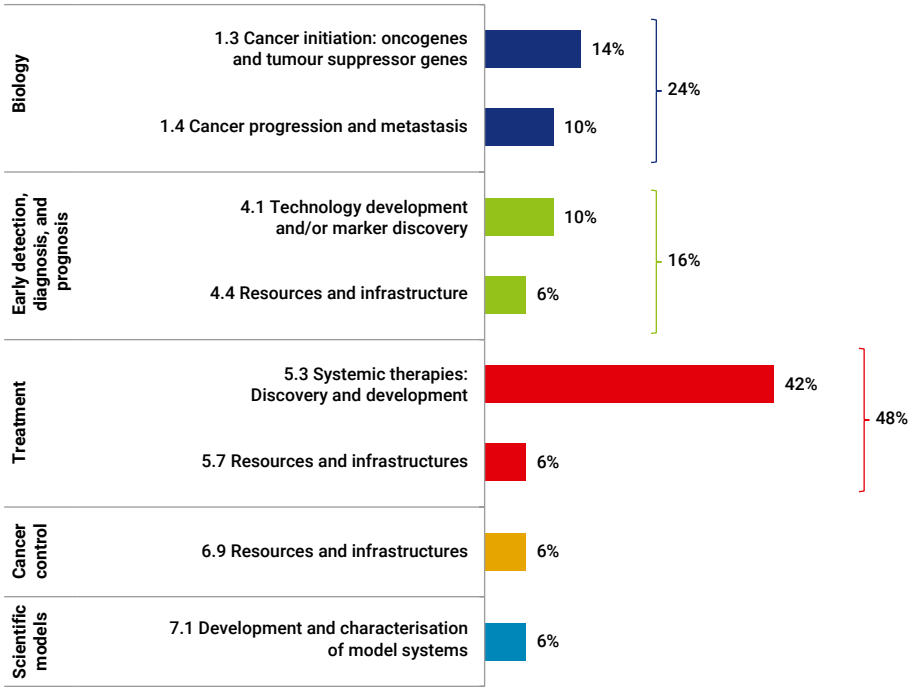
Objectives	To promote training of students or young medical, pharmacy and veterinary science graduates in translational research by funding doctoral theses on cancer.
Programming institution	ITMO Cancer-Aviesan
Operating institution	Inserm
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€1.2M**
Proposals evaluated	**33**
Projects funded	**8**
Funding rate	**24%**

The projects funded in 2022 had the following objectives: validate biomarkers predictive of response or resistance to immunotherapy in non-small cell lung cancer; understand the role of mucosal-associated invariant T-cells (MAIT) in haematopoietic stem cell allografting as a treatment for acute myeloid leukaemia; understand the role of tumour cells and the microenvironment in inflammation during Waldenström disease; characterise the oncogenic network involved in the early stages of TLX3-related T oncogenesis in acute lymphoblastic leukaemia; assess the impact of genetic instability associated with DNA damage response and repair (DDR) defects on the response to immunotherapy; design organoid models of high-grade gliomas to understand the development of resistance and test new therapeutic combinations; analyse tumour residue and its microenvironment

to characterise metastatic recurrence in triple-negative breast cancer; understand and model the attenuated phenotype of Fanconi anaemia *in vitro* and *in vivo*; study the mechanism of action of the anti-CD3/CD20 bispecific antibody in a B lymphoma context; synthesise inhibitors of casein kinase 2 subunit interaction and evaluate their anticancer activity in 2D and 3D models of renal cancers; characterise the interactions between acute myeloid leukaemia cells and their microenvironment in a humanised mouse model; describe, at the single cell level, the dynamics of transcriptomic (coding and non-coding RNAs) and epigenomic modifications in cancers treated with anti-PARP.

FIGURE 14

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PHD TRAINING PROGRAMME PROGRAMME(FRFT-DOC) IN 2022 ACCORDING TO THE CSO CLASSIFICATION



SUPPORT FOR THE INTERDISCIPLINARY RESEARCH PROGRAMME OF THE "FAN" DOCTORAL SCHOOL BY ITMO CANCER-AVIESAN

The "Frontières de l'innovation en recherche et éducation" (FIRE) doctoral school is an international and interdisciplinary PhD programme, hosted by Université Paris-Cité and co-hosted by Université Paris Sciences et Lettres (PSL), that promotes original and ambitious research projects involving interactions between a wide range of academic disciplines. Research projects belong to one of two tracks: FdV (Frontières du vivant) and FAN (Frontières de l'apprendre et du numérique). Since 2010, ITMO Cancer-Aviesan has supported cancer projects within the framework of the FIRE programme belonging to either the FdV or FAN tracks.

2022:
1
project funded
for a total amount of
€108,000

TABLE 17
FEATURES OF THE TRAINING IN INTERDISCIPLINARY RESEARCH – FRONTIÈRES DE L'INNOVATION EN RECHERCHE ET ÉDUCATION (FIRE) PARTNERSHIP IN 2022

Objectives	To promote ambitious cancer research projects using a broad range of academic disciplines
Programming institution	FIRE graduate school
Operating institution	FIRE graduate school
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€108,000 (1 project)**

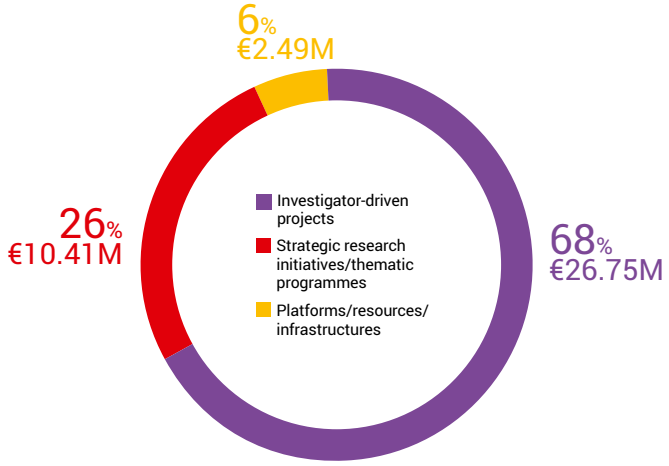
The project funded in 2022 belonged to the FAN track. It was aimed at dissecting the response of the tumour microenvironment to nanoparticles-mediated hyperthermia (HT) combined with anti-cancer drugs in tumour-on-chip devices.

CLINICAL CANCER RESEARCH AND ACCESS TO INNOVATION

Within the framework of the successive Cancer control plans, INCa has implemented several actions to support clinical research through calls for proposals, specific programmes to roll out targeted therapies and personalised medicine and the setting up of specific infrastructures. In addition, support for clinical research has been extended through international collaborations, the establishment of public-private partnerships, and support for access to innovation.

In 2022, support for clinical cancer research amounted to:

€39.66M



National Clinical Research on Cancer

NATIONAL PROGRAMME FOR HOSPITAL CLINICAL RESEARCH ON CANCER (PHRC CANCER)

Nationwide support of academic clinical cancer research is organised through a specific call for proposals operated by INCa, and funded by the Direction of French Ministry of Health DGOS: the national programme for hospital clinical research on cancer or PHRC cancer (PHRC-K).

- PHRC-K funds clinical cancer research projects with the following objectives:
  - assessment of the efficacy of health technologies. To meet this objective, priority is given to funding research that, using controlled comparative methods, randomised or not, should help achieve recommendations with strong scientific evidence;
  - evaluation of the safety, tolerance or feasibility of the use of health technologies in humans.
- In accordance with the Ten-year cancer control strategy and the previous cancer control plans, the objectives of the PHRC-K programme are particularly:
  - reduction of the toxicity of treatments in the medium and long term and its assessment in adults, young adults and children (**de-escalation trials**, see below);
  - areas pertaining to advanced forms of tumour diseases, oncogeriatrics and paediatric oncology;
  - research projects addressing individual or collective behavioural changes, or exploring drug-based approaches in the prevention of cancer risks;
  - projects that include assessment of patients' quality of life (during and/or after illness);
  - combination of several targeted drugs, or combinations of targeted drugs with chemotherapy or radiotherapy;
  - clinical validation of the efficacy of innovative health technologies for treatment or diagnosis;
  - increase in patient survival;
  - Evaluation of treatment- or disease-related sequelae, and means for reducing them;
  - supportive care, palliative care and end of life;
  - meta-analyses addressing controversial issues in treatment efficacy;
  - strong participation from major cooperative groups is expected, particularly with regard to proposing and conducting clinical trials aimed at addressing the major therapeutic questions of increasing survival and reducing the side-effects and delayed effects of treatments;
  - research in primary care and prevention (French national health strategy).

Reducing the toxicity of treatments in the medium and long term is part of an approach to reduce sequelae and improve patients' quality of life. This approach is one of the key priorities of the Ten-year cancer control strategy. Therapeutic de-escalation trials are particularly expected and, in the context of the Ten-year cancer control strategy, are treated as a priority.

In 2021-2022, 176 letters of intent were submitted to PHRC-K and 36 projects were selected for funding for a total amount of €26.7M (Table 18).

2022:
36 clinical research projects funded out of the **176** submitted for a total budget of **€26.7M**

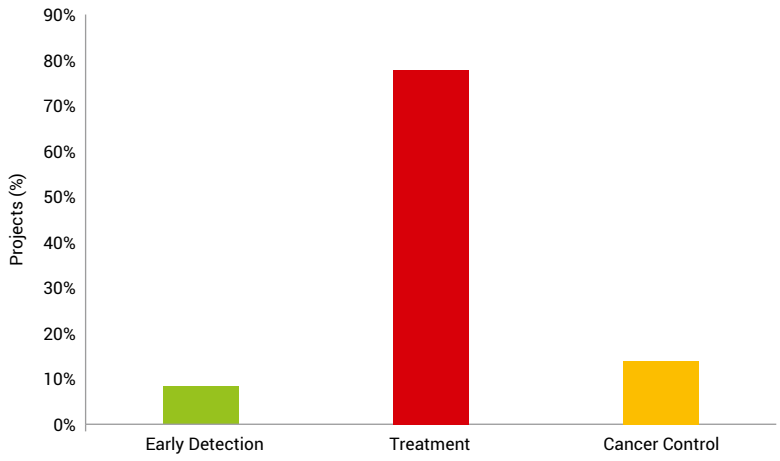
TABLE 18
FEATURES OF THE PHRC-K PROGRAMME IN 2022

Objectives	• To assess the efficacy of health technologies; • To evaluate safety, tolerance or feasibility of the use of health technologies in humans.
Programming institution	INCa/Ministry of Health (DGOS)
Operating institution	INCa
Funding institution	Ministry of Health (DGOS)
Funding	**€26.7M**
Proposals submitted	**176**
Projects selected	**36**
Selection rate	**20%**

For 2022, the CSO analysis of funded projects shows that the majority of the funded projects belong to the treatment category (77.8%) and, particularly, to clinical applications of systemic and localised therapies (66% and 14.3%, respectively). The other topics studied are related to early diagnosis (8.3%) and care and survivorship (13.9%) (Figure 15).

Amongst the funded projects, **7** were de-escalation trials for a total amount of **€6.5M**

FIGURE 15
DISTRIBUTION OF SELECTED PROJECTS ACCORDING TO THE CSO CLASSIFICATION IN 2022



PHRC-K programme – report workshops

In 2022, the French National Cancer Institute (INCa) organised 3 report workshops as part of annual French-speaking conferences of 3 disciplines: radiotherapy, imaging, and supportive cancer care.

In addition to presenting the results of funded projects, these workshops allow us to obtain feedback concerning sources of leverage and difficulties in implementing clinical research projects.

"PHRC-K in radiotherapy, experience feedback" workshop – September 2022
This workshop was organised as part of the French Society of Radiotherapy in Oncology (SFRO) and provided an opportunity to present 4 projects:

Lung Art: Phase III study comparing post-operative conformal radiotherapy to no post-operative radiotherapy in patients with completely resected non-small cell lung cancer (NSCLC) and mediastinal N2 involvement, by Cécile Le Péchoux (Villejuif, PHRC-K 2012).
The results of this study were published in the Lancet Oncol in January 2022.

STEREO-POSTOP-01: STEREO-POSTOP-01
A multicentre prospective phase II study of postoperative hypofractionated stereotactic body radiotherapy (SBRT) in the treatment of early stage oropharyngeal and oral cavity cancers with high risk margins, by Julian Biau (Clermont Ferrand, PHRCK 2016).
The results of this study were published in BMC Cancer in August 2020.

ARTOME: Health economics evaluation of the adaptive radiotherapy strategy to decrease xerostomia in locally advanced oropharynx carcinoma, by Renaud de Crevoisier (Rennes, PRME K 2014).
This study is currently being finalised.

CONCORDE Prodige 26 : Radiochemotherapy with or without radiation dose escalation in patients with locally advanced or inoperable esophageal carcinoma: Phase II-III trial (PHRC-K 2009)
The results of the CONCORDE study were published in Radiotherapy and Oncology in August 2015 and in International Journal of Radiation Oncology Biology Physics in 2021.

OLIVER: Oligometastases of the LIVer treated with chemotherapy with or without Extracranial Stereotactic Body Radiation Therapy in patients with colorectal cancer (PHRC-K 2015), by Gilles Créhange (Institut Curie, Paris).
The project was stopped prematurely due to implementation difficulties.

"Multimodal imaging in cancer – Update of knowledge based on the results of recent PHRC-K/STIC" workshop – October 2022
This workshop organised as a part of the conference of Journées Francophones de la Radiologie (JFR) in October 2022 presented the following projects :

IRCIS: Evaluation of the performance of MRI+biopsy in optimising surgical excision of ductal carcinoma in situ (DCIS) of the breast, by Corinne Balleyguier (Gustave Roussy, PHRC-K 2009).
The results of this study were published in the Journal of Clinical Oncology in 2019 and in the European Journal of Radiology in 2020.

EVALICEMM: Evaluation of dynamic MRI with contrast injection as an independent prognostic factor for relapse-free survival in multiple myeloma after therapeutic intensification and hematopoietic stem cell autotransplantation, by Sébastien Mulé/Alain Luciani (AP-HP, PHRC-K 2009).
The results of this study are not published yet.

IMAJEM: Medico-economic evaluation of the interest of FDG-PET in patients with multiple myeloma, under 65 years of age, treated in the IFM 2009-01 protocol, by Françoise Kraeber-Bodéré/Philippe Moreau (CHU Nantes, STIC 2010).
The results of this study were published in Journal of Clinical Oncology in 2017 and 2021, and in Cancers in 2020.

CorticoTEP: Performance of 18F-Fluorodeoxyglucose positron emission tomography (FDG-PET) in the diagnosis of indeterminate adrenal tumours on

conventional imaging: A French prospective multicentric study, by David Taieb (AP-HM, PHRC-K 2010).
The results of this study were published in Journal of Clinical Endocrinology and Metabolism in 2017 and in Clinical Endocrinology in 2021.

Evaluation of a new PET tracer: O-2 18F fluoro-ethyl-tyrosine, or FET, in the management of low-grade gliomas, by Pierre Payoux (CHU Toulouse, PHRC-K 2008).
The results of this study have not been published.

"Hospital programme for clinical research in supportive cancer care" workshop – October 2022
In order to illustrate the PHRC-K programme's support for supportive and palliative care, a specific seminar devoted to this field was organised as part of the Association Francophone des Soins Oncologiques de Support (AFSOS) conference, in October 2022. During this seminar, two PHRC-K projects were reported:

PALLU: A prospective multicentre study of the efficacy of systematic screening of the need for palliative care during an unscheduled visit on the aggressiveness of care in patients nearing end of life in comprehensive anticancer centres, by Gisèle Chvetzoff (Lyon, PHRC-K 2022).

Cog-stim2: Remotely coached computerised cognitive remediation to reduce post-chemotherapy cognitive difficulties in patients treated for localised breast cancer. a multicentre randomised controlled trial, by Florence Joly (Caen, PHRC-K 2022).

Utilisation of projects funded or supported by INCa's programmes

Results of the FIRSTMAPP trial
FIRSTMAPPP is the first academic randomised double-blind phase II study assessing Sunitinib efficacy compared to placebo in patients with a very rare cancer -Malignant pheochromocytoma and paraganglioma (MPP). This project was awarded funding by PHRC-K in 2011. A total of 78 patients were enrolled for 8 years in 15 French and European centres.

The FIRSTMAPP results validated, after 8 years of enrolment, with the highest possible level of evidence, treatment with Sunitinib. The results of FIRSTMAPP[1] were presented at the ESMO conference in September 2021. In February 2022, INCa interviewed the PI of the trial, Prof. Eric Baudin (Gustave Roussy): https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Cancers-ultra-rares-resultats-de-l-etude-FIRSTMAPPP-financee-par-le-PHRC-K.

Results of the Lung ART trial
Lung ART is a European academic, open-label, randomised, phase III trial intended to establish whether postoperative radiotherapy should be part of their standard treatment in patients with non-small-cell lung cancer (NSCLC). This project was awarded funding by PHRC-K in 2012. A total of501 patients were enrolled between 2007 and 2018 in 64 centres in 5 European countries (France, UK, Germany, Switzerland and Belgium).

The Lung ART results demonstrated that conformal postoperative radiotherapy cannot be recommended as the standard of care for patients with stage IIIAN2 NSCLC.

The results of Lung ART were presented at the ESMO conference in 2020 and published[2] in January 2022 in The Lancet Oncology. In July 2022, INCa interviewed the PI of the trial, Dr. Cécile Le Péchoux (Gustave Roussy): https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Cancers-du-poumon-une-etude-financee-par-un-PHRC-K-pour-determiner-l-efficacite-de-la-radiotherapie-post-operatoire

Results of the ENDOLA trial
ENDOLA is an academic, early phase I/II clinical trial sponsored by Hospices Civils de Lyon and funded in 2016 by INCa as part of the specific call for proposals

[1] Eric Baudin et al. First International Randomized Study in Malignant Progressive Pheochromocytoma and Paragangliomas (FIRSTMAPPP): An academic double-blind trial investigating sunitinib. Abstract ESMO 2021.
[2] Cécile Le Péchoux et al. Postoperative radiotherapy versus no postoperative radiotherapy in patients with completely resected non-small-cell lung cancer and proven mediastinal N2 involvement (Lung ART): an open-label, randomised, phase 3 trial. The Lancet Oncology. January 2022.

on innovative drugs, through a partnership with AstraZeneca. The ENDOLA study was conducted from 2016 to 2021 in 6 CLIP[2] centres in France and included 31 patients.

The ENDOLA results demonstrated good safety and efficacy of olaparib combined with two other molecules aimed at limiting the growth of metastatic endometrial cancer with acceptable side-effects.

The results of ENDOLA[3] were presented at an AACR plenary session in April 2022.
In October 2022, INCa interviewed the PI of the trial, Prof. Benoît You (Hospices Civils de Lyon): https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Cancers-avances-de-l-endometre-une-etude-financee-par-l-Institut-demontre-l-efficacite-d-une-combinaison-de-traitements-sans-chimiotherapie-agressive

[3] Benoit You et al. CT005 – Safety and efficacy of olaparib combined to metronomic cyclophosphamide and metformin in recurrent advanced/metastatic endometrial cancer patients: ENDOLA trial. Abstract AACR 2022.

Clinical cancer research status report

In 2021, the Institute launched a status report on academic and industrial clinical cancer research, which led to a report with conclusions identifying areas for improvement. Workshops were organised around these areas with all the stakeholders in clinical research in order to identify ways of improving clinical cancer research.

Between March and May 2022, 5 workshops involving institutional representatives, academic researchers and representatives of the pharmaceutical industry were organised on 5 topics.

Workshop 1: Funding strategy
- Optimisation of the funding strategy for academic clinical research.
- Mobilisation and encouragement of health professionals to invest in clinical research.

Workshop 2: Organisation of clinical research and patient experience
- Reduction of inequalities in access to trials.
- Improvement of the patient experience.

Workshop 3: Public-private articulation
- Strengthening public-private cooperation around common projects to increase the attractiveness and impact of clinical research in French cancer research.

Workshop 4: Improvement of the launch process, from funding to inclusion of patients
- Optimisation and improvement of clinical trial launch process.

Workshop 5: Innovation and new technologies
- Supporting the deployment of innovations in methodologies, organisations and access to therapeutic innovations.

These workshops proposed 28 recommendations classified into 7 categories helping identify new and implementable actions.

Categories of recommendations	Number of recommendations
Optimisation of the funding strategy for academic clinical cancer research	4
Optimisation of the trial initiation process	5
Mobilise and encourage healthcare professionals to be involved in clinical research	3
Reducing inequalities in patient access to cancer clinical trials	4
Improving the experience of patients included in cancer clinical trials	3
Strengthening public-private cooperation on joint projects to increase the attractiveness and impact of French clinical cancer research	3
Support the deployment of innovations in methodologies, organisations and access to therapeutic innovations.	6

SUPPORT FOR CLINICAL RESEARCH IN FRENCH OVERSEAS DEPARTMENTS

INCa has provided financial support to enable the development of clinical research in these territories, particularly for opening investigation centres, as part of the implementation of the 2014-2019 Cancer Control Plan in French overseas departments. This action is now fully part of the 2021-2030 Cancer Control Strategy within the framework of Area 3, "Addressing poor-prognosis cancers", and Action 5.2 "Offering all patients the possibility of taking part in clinical trials, opening up trials to more centres including those in overseas territories, while ensuring the quality of these centres for clinical research".

For this purpose, INCa and the Interregional Group for Clinical Research and Innovation for Southwest and Overseas Hospitals (GIRCI SOHO) have identified projects suitable for opening investigation centres in French overseas departments. GIRCI SOHO includes the 3 overseas University Hospitals (CHU Martinique, CHU Guadeloupe, CHU La Reunion), as well as healthcare centres.

In 2019, 7 projects were proposed for total funding of around €300,000 for 1, 3 or 4 years, which should enable 104 patients to be enrolled in clinical cancer trials in French overseas departments (colon cancer, head and neck cancer, cervical cancer, and leukaemia) (Table 19).

A press release was published on 21 September 2022 named "Inclusions of patients in cancer clinical trials in the French overseas territories: the French National Cancer Institute and the GIRCI SOHO draw up a first assessment " https://www.e-cancer.fr/Presse/Dossiers-et-communiques-de-presse/Inclusions-de-patients-dans-des-essais-cliniques-en-cancerologie-en-Outre-Mer-l-Institut-national-du-cancer-et-le-GIRCI-SOHO-dressent-un-premier-bilan.

It was thus decided to make this action long-term with the aim of identifying new projects in 2022, evaluated within the framework of previous calls for proposals such as PHRC-K.

TABLE 19

FEATURES OF THE CLINICAL RESEARCH PROJECTS SUPPORTED IN FRENCH OVERSEAS DEPARTMENTS AND ENROLMENT STATUS IN 2019 (DECEMBER 2022)

Projects	Funding	Duration of the project	Investigation centres	Number of patients to be enrolled	Number of inclusions December 2022
LEANOX LEAn Body Mass Normalisation of OXaliplatin Based Chemotherapy for Stage III Colon Cancer Patients Treated in Adjuvant Setting: Impact on Oxaliplatin-induced Sensitive Neurotoxicity. A Multicentre Phase II Randomised Trial.	€25,915	36 months	CHU Martinique	25	1 (*study closed for inclusions*)
SIMPA-01 Efficacy of an Oral Immunomodulatory Nutrient on Survival During Postoperative Concomitant Chemoradiotherapy in Head and Neck Cancer.	€57,614	48 months	CHU Martinique CHU La Réunion Clinique Ste Clotilde	12 15 12	– stopped
EMUTRAS Detection of the Emergence of RAS Mutations in Circulating DNA in Patients With Metastatic Colorectal Cancer During Treatment With Anti-EGFR Therapy.	€10,248	36 months	CHU Martinique CHU La Réunion	10 3	2
OPEN Trismus Prevalence and Preventive Rehabilitation Associated With Therapeutic Education for Patients With Head and Neck Cancer Treated With Concomitant Radiochemotherapy.	€5,936	12 months	CHU La Réunion	5	2
ONCOCOL Phase III Study Comparing Neoadjuvant Chemotherapy with Carboplatin and Paclitaxel Followed by Standard Therapy, With Standard Therapy Alone in Women With Cervical Cancer and Para Aortic Positive Lymph Node.	€68,871	48 months	CHU Guadeloupe	6	– Centre to be opened
DEXAML-03 Dexamethasone Plus Salvage Chemotherapy Versus Salvage Chemotherapy Alone in Patients with First Relapsed or Refractory Acute Myeloid Leukaemia: a Randomised, Controlled, Open-label, Multicentre, Phase III Study.	€29,000	48 months	CHU La Réunion	6	2
ONCOGRAM Study of the Therapeutic Response and Survival of Patients with Metastatic Colorectal Cancer (Stage IV) and Treated According to the Guidelines of a Chemosensitivity Test, Oncogramme®.	€94,455	36 months	CHU Martinique	10	9

Public-private partnerships

Since 2011, INCa has promoted early access to innovative drugs for patients through cooperation with pharmaceutical laboratories (cooperation agreements) who supply and distribute innovative molecules to the CLIP² network. This access to drugs in development enables institutional investigators to propose academic clinical trials for indications or diseases not addressed by pharmaceutical laboratory development plans.

These trials, designed and proposed by CLIP²s, are aimed at promoting the early development of new therapeutic strategies, in indications which would probably not have been investigated by pharmaceutical firms, for the benefit of patients.

THE PROGRAMME IN 2022

In May 2021, INCa signed a new agreement with Merck to provide the 16 CLIP² centres with four innovative drugs:

- Peposertib (M3814): DNA-PK inhibitor;
- Berzosertib (M6620): ATR inhibitor;
- Tepotinib: MET inhibitor;
- M1774: ATR oral inhibitor.

This agreement enabled the launch of a call for proposals in June 2021. Among the 22 projects submitted in total by 16 CLIP² centres, 4 will be funded for a total amount of €3.17M.

TABLE 20
FEATURES OF THE EARLY PHASE CLINICAL TRIALS CALL IN 2022

Objectives	The purpose of this call for proposals is to select, based on applications, early phase clinical trial proposals aimed at assessing the drugs, Peposertib (M3814), Berzosertib (M6620), Tepotinib, M1774, administered in mono or combination therapy.
Programming and opérating institution	INCa
Funding institution	INCa/ARC Foundation
Funding	**€3.17M** **INCa: €2.73M** **ARC Foundation: €0.44M**
Proposals submitted	**22**
Projects selected	**4**
Selection rate	**18%**

Public and private partnerships – new call for proposals on innovative drugs

In 2022, the Institute and the pharmaceutical company Amgen signed a collaboration agreement to make innovative drugs available to the CLIP² network. Most of these innovative drugs from the Amgen development pipeline are still in the early development phase and thus have not yet received marketing approval. The three proposed molecules are:

- Sotorasib: KRASG12C inhibitor
- Tarlatamab (AMG 757): CD3/DLL3 bispecific antibody
- Bemarituzumab (AMG 552): Anti-FGFR2b antibody

After signing this agreement, the Institute published a call for proposals for the 16 CLIP² centres in November 2022. The selection of projects will proceed in 2023.

TABLE 21
CHARACTERISTICS OF THE SELECTED PROJECTS

Agents	Title	CLIP² centre and PI
Peposertib : DNA-PK inhibitor – Merck **Avelumab: Anti PD-1 antibody – Merck** **Metronomic Temozolomide**	Phase 1/2 evaluating a combination of metronomic temozolomide, avelumab and peposertib in children and adolescent with refractory/relapsing tumours – A new arm of the AcEs-ESMART trial.	CLIP²: Centre d'Essais Précoces en Cancérologie de Marseille AP-HM – Hôpital de la Timone – MARSEILLE Prof. Nicolas ANDRE
M1774 : ATR oral inhibitor – Merck **fulvestrant**	MATRIx: a phase I/II study evaluating **M**1774, an **ATR I**nhibitor, in combination with fulvestrant in hormone receptor-positive and HER2-negative, advanced breast cancers, resistant to CDK4/6 inhibitor plus aromatase inhibitor-based endocrine treatment and with homologous recombination deficiency, oncogenic driver activation and/or other molecular alterations associated with replicative stress	CLIP²: Institut Paoli-Calmettes Institut Paoli-Calmettes – MARSEILLE Prof. Anthony GONCALVES
M1774 : ATR oral inhibitor – Merck **PLX038 (Topo1 inhibitor)**	A Phase I Study on M1774 (oral ATR inhibitor) in Association with PLX038 (Topo1 inhibitor) in patients with advanced triple-negative breast cancer or advanced cancer with ATM mutation	CLIP²: D³i Department of Drug Development & Innovation Institut Curie – PARIS Prof. François-Clément BIDARD
M1774 : ATR oral inhibitor – Merck **Niraparib : PARP inhibitor – GSK** **Dostarlimab: anti-PD-1 antibody – GSK**	Intermittent dosing of the ATR inhibitor M1774 in combination with niraparib and dostarlimab in selected solid tumours: a dose-escalation and proof-of-concept phase 1 study	CLIP²: GUSTAVE ROUSSY Institut Gustave Roussy – VILLEJUIF Dr. Sophie POSTEL-VINAY

THE PROGRAMME OVER THE 2010-2022 PERIOD

From the beginning of the programme up to the end of 2022, INCa launched 17 specific calls for proposals to propose 44 drugs under development, 37 projects were selected, and 28 of these were funded for €17.85M; 17 were co-funded by the ARC Foundation.

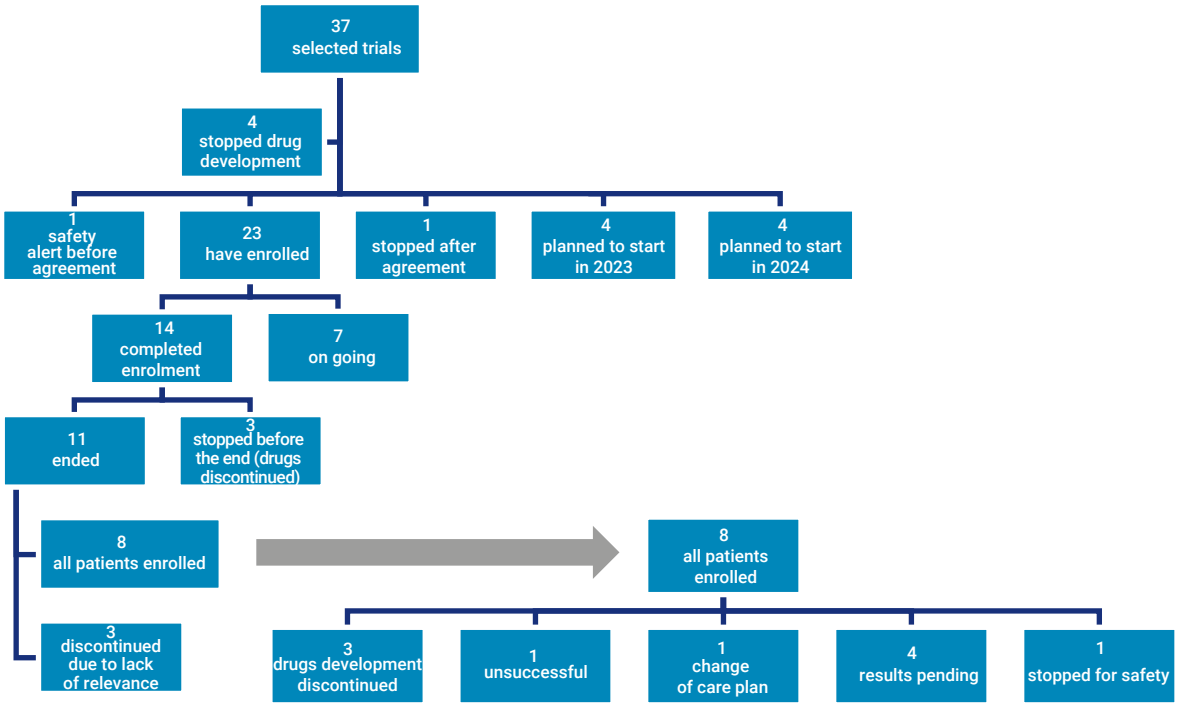
INCa Funding: €12.31 M

ARC Foundation funding: €5.54 M

By the end of 2022, 23 projects had started to enrol patients and the 4 other recently selected projects were planned to commence in 2022.

FIGURE 16

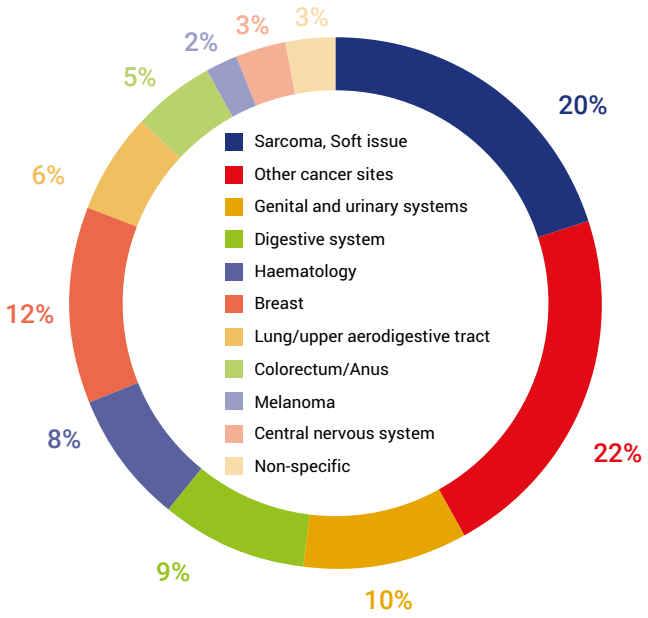
OUTCOMES OF SELECTED PROJECTS (TRIALS)



In this programme, the trials which were able to commence have included at least 850 patients so far.

The distribution of the funding of the projects highlights the specificity of this programme, with a large proportion of rare diseases. Trials addressing sarcoma and soft tissue represent more than 20% of the funded projects compared to the PHRC-K programme where they account for 8% and where haematology constitutes a large proportion of the funding.

FIGURE 17
DISTRIBUTION OF THE SELECTED EARLY CLINICAL TRIALS ACCORDING TO THE CANCER SITES STUDIED OVER THE 2011-2022 PERIOD



Precision medicine initiatives

CAR T-CELLS – T2EVOLVE

INCa is participating in T2EVOLVE "Accelerating development and improving access to CAR and TCR engineered T-cell therapy", a European Joint Undertaking led by the Innovative Medicines Initiative (IMI). The IMI is an EU public-private partnership funding agency whose mission is to improve health by speeding up the development of, and patient access to, innovative medicines, particularly in areas where there is an unmet medical or social need. IMI is currently transitioning to the Innovative Health Initiative (IHI).

Operationally launched in January 2021, T2EVOLVE is a 5-year project. Under the co-leadership and the coordination of Prof. Michael Hudecek, MD (Universitätsklinikum Würzburg, Germany) and Dr. Hélène Negre, PhD (Servier Iris and European Federation of Pharmaceutical Industries and Associations (EPFIA) project leader), T2EVOLVE is aimed at identifying opportunities at both National and European levels, to accelerate research and development on engineered T-cell therapy and improve patient access to these innovative treatments. With the participation of various stakeholders in the field, several topics are being addressed, such as the development of engineered T-cells by early-stage developers (academics and start-ups), the manufacture of engineered T-cells at "point-of-care", health technology assessment (HTA), pricing and reimbursement pathways for engineered T-cells.

INCa is task leader in two work packages (WP):

- WP2 which specifically addresses the need for patient information, engagement and involvement in healthcare decisions in the field of engineered T-cells;
  - the first objective of this WP is to deliver 5 explainer videos intended for patients and carers. The second objective is to provide recommendations to healthcare professionals for more patient-friendly informed consent forms (ICFs). The final objective is to present a roadmap listing the potential opportunities that could help ensure a safe, effective, quick, broad, equitable and sustainable access to engineered T-cell therapy to European institutions (European Parliament, European Commission and European Medicine Agency), as well as all possible stakeholders involved in the field of engineered T-cells at a national level.
- WP5 which addresses needs for standardisation of analytical practices in this field, in the aim of improving prediction and comparison of safety and efficacy of the products;
  - the objective of this WP is to deliver guidelines for standardisation of analytical assays which will be widely distributed to key stakeholders in Europe.

Achieved milestones of the project and INCa-led tasks

- ***WP2: Patient engagement***

INCa has contributed to the development of a working group of patients and caregivers (WGPC). This group allows the consortium to orientate its work according to the patients' perspective and feedback. Four meetings of the WGPC were held between May 2021 and September 2022 during which we (i) co-developed a European survey on the experience of patients treated with engineered T-cell therapy; (ii) participated in the inventory of educational material for patients and healthcare professionals as well as its review according to the PEMAT (Patient Education Materials Assessment Tool) standardised approach. Since December 2022, references to these materials can be found on the T2EVOLVE website, in the "patient hub" section; (iii) identified 5 topics for explainer videos; (iv) delivered the working plan for the "access roadmap".

- ***WP5: Standardisation of analytical practices***

Under the leadership of INCa, a Committee of European National Experts on engineered T-cells (CENET) has been created, including 15 experts from 14 different countries. Two meetings were held in 2021 during which feedback from CENET members were collected to finalise the drafting of the European survey on current analytical practices in the field of engineered T-cells. Two other meetings were held in 2022 during which not only results from the WP5 European survey but also progresses made in the different WP5 working groups (immunomonitoring and potency assays) were presented to CENET members.

In parallel with this survey, INCa is involved in the drafting of the standardisation approach that WP5 members are seeking to apply to several analytical assays used to control engineered T-cell products. Standardisation guidelines are expected to be shared and distributed across Europe by the end of the project in 2025.

2023 INCa-led milestones and deliverables

At the beginning of 2023, INCa will help disseminate the European survey on the experience of patients treated with engineered T-cell therapy. Based on the results of the survey, INCa will draft recommendations to make ICFs more patient-friendly. INCa will lead the creation of the first 3 explainer videos intended for patients and carers, and will address topics for which patients treated with engineered T-cells from WGPC identified a need for information. In the course of the year, INCa will also be conducting individual interviews with public and private stakeholders involved in the field of engineered T-cells to identify the current hurdles impeding access to CAR T-cells. Based on results of the interviews, 3 major topics will be selected in order to organise 3 separate thematic workshops with key stakeholders to find new opportunities and start drafting an "access roadmap" to improve patient access to engineered T-cell therapy across Europe further. Thematic workshops are expected to be held by the end of 2023.

Meanwhile, INCa will lead the analysis of the WP5 European survey on analytical standards. The first submission of the manuscript in *Frontiers in Immunology* is expected in Autumn 2023.

MOLECULAR SCREENING-BASED CLINICAL TRIALS

Since 2017, the Institute, in collaboration with CLIP² coordinators, has provided a tool to identify clinical trials requiring the presence of one or more specific biomarkers. This kind of information was not previously available, but it is now strongly recommended to guide patients into the most relevant clinical trials, considering the new kind of drugs tested, the implementation of NGS (Next Generation Sequencing) in routine clinical practice in molecular genetic centres, as well as the multiplication of molecular screening programmes on large panels of genes developed in many centres.

Thus, the Institute has drawn up a list of clinical trials with molecular screening conducted within CLIP² centres. Initially focused on early-phase trials, this list is now extended to all phase trials to ensure access for all patients.

In order to obtain an up-to-date list, a survey is carried out three times a year on CLIP² centres, in order to introduce the new trials opened and to withdraw the trials closed for inclusion.

In 2022, a new tool was introduced to make it easier for all those involved in clinical research, investigators, carers and molecular biologists, to view and search for trials with molecular screening.

This tool is available at: https://dataviz.e-cancer.fr/app/06-DATAVIZ_SCREEN/

Once the data is updated, an information e-mail is sent to the investigators and members of the Molecular Tumour Boards (about 350).

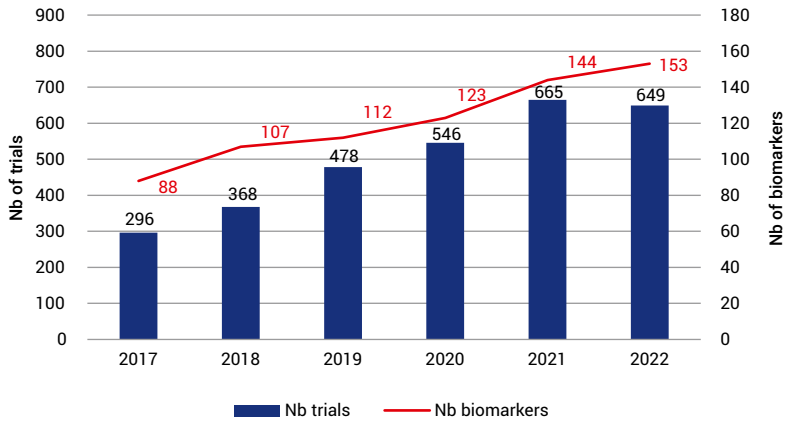
This visualisation tool includes a search engine that allows the selection of trials according to any of the displayed criteria, primarily the biomarker and the associated biological alteration. A link to the clinical.gov website provides users with more information if needed.

Issuing recommendations for the prescription of somatic testing

The landscape of molecular somatic testing in cancer is becoming increasingly complex and it is required to issue recommendations for the prescription and/or the procedures involved in these tests to guide professionals in their practice and ensure the best possible care for patients in France. Accordingly, the Institute has been working with experts to issue several recommendations.

To ensure that each patient get all the necessary tests for optimal care and to optimise the number of tests performed in France yearly, INCa has set up working groups with pathologists, molecular geneticists and clinicians to produce recommendations for the prescription of somatic tests for cancer. The aim is to list all the different stages of the disease and to recommend which test should be carried out at which stage to ensure the best diagnosis or treatment for each patient. The colon cancer document was published in 2022 while recommendations about lung cancer and melanoma are in preparation.

FIGURE 18
PROGRESSION OF THE NUMBER OF TRIALS AND BIOMARKERS IN THIS LIST



Results of the study on the inventory and assessment of the national oncogenetics system (consultations and follow-up)

Context

Nearly 5% of diagnosed cancers are related to hereditary predisposition to cancer. Screening for a genetic predisposition to cancer makes it possible to identify a population at risk, adapt surveillance, and personalise treatment. In France, the diagnosis of these predispositions is implemented within the framework of the national oncogenetics system. In 2020, this system was organised around 146 consultation sites in 101 towns and cities throughout France (metropolitan France and overseas departments). These sites work in close collaboration with the laboratories in charge of carrying out genetic tests prescribed during consultations. To complete this system, 17 regional and interregional programmes have been set up to coordinate and facilitate the follow-up of people at very high risk of cancer once families have been identified.

From 2003 up to the COVID-19 pandemic, the number of oncogenetics consultations continued to increase, on one hand because new families with a hereditary predisposition to cancer had been identified and the criteria for accessing this type of consultation are now better known by health professionals, and on the other because oncogenetics consultations now play a central role in the care pathway for patients. This activity can only continue to increase with the development of precision medicine and the implementation of "Plan France Médecine Génomique 2025" a French initiative for genomic medicine.

As part of the 2021-2030 national cancer control strategy (*action II.3.3 Making precision medicine accessible to all*), actions have already been taken to strengthen the oncogenetics offering:

- working with DGOS of the French Ministry of Health, which led to an additional €2M being added to the oncogenetics general interest mission (MIG; mission d'interêt general) at the end of 2021;
- **the study on the inventory and assessment of the national oncogenetics system** (initial consultations and follow-up programmes), by measuring the efficiency of the system and by proposing an organisation and financing system that is better adapted to recent and expected developments in the oncogenetics pathway. This study was

launched in November 2021 with the service provider EuroGroup Consulting and ended in December 2022.

Major points of the diagnosis and main recommendations:

1. A lack of strategy and steering of oncogenetics at a national level, resulting in poorly defined objectives and missions, a lack of efficiency and quality management and heterogeneous practices.
Recommendations: a) determine the strategic objectives of the national oncogenetics system for the coming years, b) validate and set up a steering committee and a monitoring committee, and c) determine the relevant indicators for monitoring the activity and quality of the oncogenetics offering.

2. An unmanaged funding model:
The budgets allocated to consultations are partially correlated to activity and do not take into account the quality of care. Furthermore, coding practices vary greatly from one institution to another.
Recommendations: 1) make funding more equitable and support increased quality of care. 2) continue discussions with DGOS on the evolution of the funding model and 3) promote the harmonisation of coding practices.

3. Inequalities in access to the system based on locality:
Major regional disparities, both because of unequal regional coverage in terms of the number of consultation sites, but also because of heterogeneity in the number of consultations carried out in relation to the population and the incidence of cancers in different regions. The provision of follow-up for high-risk individuals is also heterogeneous, with different types of organisation, but the lack of precise and objectively verifiable indicators does not allow a true evaluation of the missions.

4. Team organisation varies greatly, with no one model being more efficient than others:
This heterogeneity would seem to stem more from operating methods and practices that vary according to the local organisation than from a specific team composition. Medical time is greater than or equal to genetic counselling time in the vast majority of networks, and is largely dedicated to consultations.

Main recommendations for improving system organisation

For initial consultations:

- extend the implementation of accelerated management procedures that allow urgent access to consultations (average time of 10 days compared to 18 weeks for other index cases), as well as pre-consultation procedures and prioritisation of requests in order to improve the patient referral process towards classic or emergency consultation;
- medical time could be optimised further, notably by strengthening the role of the genetic counsellor;
- increasing the number of medical assistants is also a possible key to gaining time and efficiency, especially during the first consultation for new patients, which lasts for an average of one hour;
- propose teleconsultation for negative results to limit patient travel.

For the follow-up of high-risk individuals:

- strengthen partnerships with primary care practitioners. The problem of medical demographics seems to be one of the main causes of the complexity of local follow-up;
- implement computer tools that are better adapted to oncogenetics;
- to prevent saturation, some centres have set up different follow-up methods based on the condition of the patients to ensure optimal follow-up of known patients and regular inclusion of new patients (ensuring that patients actually start their monitoring and checking at key ages and that they are continuing their monitoring, with different levels of support depending on the complexity of the management). This new organisational scheme could be extended to other programmes;
- increasing the number of coordinating nurses and referral nurses would make it possible to save doctors' time for simple follow-up and relieve coordinating units of saturated programmes;
- strengthen collaboration with the specific regional cancer systems, the DSRCs (Dispositif Spécifique Régional du Cancer), to identify and regularly update a list of referring practitioners;
- carry out information campaigns at a national level to make health professionals aware of the issues of high-risk individuals.

This work will serve as a basis for producing organisational guidelines (health expertise planned for 2023 and 2024 within the Organisation and Care Pathways department).

OncNGS: Development of commercial solutions for liquid biopsy diagnostics based on NGS-driven profiling

The oncNGS consortium groups eight buyers in five European countries, supported by six entities. This consortium aims to challenge the market to develop novel affordable solutions to provide the most advanced NGS tests for all solid tumour and lymphoma patients within a pre-commercial procurement Horizon-2020 financed project. INCa is one of the supporting entities of the OncNGS consortium.

The mechanism of the pre-commercial procurement is to define and launch a call for tender to develop a solution for unmet market needs in a domain of public interest. The companies selected will need to develop the solution. The tender is run in such a way that at least two different solutions must reach the market.

EU countries aim to provide equal access to innovative medicines for all, through standard care or access to clinical trials, breaking down current unacceptable inequities due to the high costs of current diagnostic/therapeutic tests. The technological challenge consists in providing efficient molecular DNA/RNA profiling of tumour-derived material in liquid biopsies by means of a pan-cancer tumour marker analysis kit, including NGS analysis integrated with a decision support system, including analytical test interpretation and reporting.

In 2022, four suppliers were selected through the call for tender to make a proposal for the solution design. In 2023, three procurers will be selected for the prototype development phase.

ACSÉ PROGRAMME

As part of the 2nd National Cancer Control Plan, the AcSé programme (Secured Access to innovative therapies) was launched by INCa in 2013, with the approval of the French Medicines Agency, to provide secured access to targeted therapies for patients in treatment failure situations, in non-authorised indications.

This programme addresses:

- safety issues, since it provides patients with controlled anti-cancer treatments based on their tumour profile and their potential molecular targets identified by one of the 28 molecular genetics centres designated by INCa, and assesses the potential efficacy and tolerance of these new therapies;
- equity of access to innovative treatments;
- the non-competition principle, since this programme is in addition to clinical trials already available and, thus, does not compete with research and development plans of pharmaceutical companies.

Since 2013, five trials have been set up:

- AcSé-Crizotinib (2013): 246 patients included/186 investigator sites/24 cohorts/completed;
- AcSé-Vemurafenib (2014): 216 patients included/118 investigator sites/11 cohorts/completed;
- AcSé-eSMART (2016): 221 children included/10 investigator sites in France/16 study arms/on-going (as of December 31, 2022);
- AcSé-Nivolumab (2017): 269 patients included/54 investigator sites/6 cohorts/follow-up;
- AcSé-Pembrolizumab (2017): 334 patients included/48 investigator sites/7 cohorts/follow-up.

LAUNCH OF THE NEW ACSÉ PROGRAMME

In 2021, as part of the Ten-Year Cancer Control Strategy, the Institute relaunched the AcSé programme, first initiated in 2013. This programme has been redefined with the help of experts from Unicancer and the French Hospital Federation Cancer brought together by the Institute. It should help address current clinical research questions raised by the latest authorised targeted therapies. Their deliberations have led them to propose four trials targeting:

- gene fusions in all cancers;
- PARP inhibitor-sensitive defects in solid tumours outside market acces;
- ErBb2 gene defects in solid or haematological cancers;
- microsatellite instabilities in all cancer except for colorectal and endometrial cancers.

These trials, in line with the initial objective of the AcSé programme, should make it possible to:

- evaluate drugs targeting a molecular anomaly in indications other than those with a marketing authorisation (MA) and provide more evidence of efficacy and comparison;
- rely on innovative methodologies and propose combinations of treatments;
- provide access to innovative treatments for patients identified in screening programmes, in particular those in the 2025 France Genomic Medicine plan.

During 2022, the experts developed the synopses for the four trials identified in 2021 and proposed the drugs that could treat the anomalies targeted by these trials to the Institute. The pharmaceutical companies that own these drugs were approached by the Institute so that they could make their drugs available to the programme. The Institute initiated a large number of discussions, mostly with the French subsidiaries of these pharmaceutical firms. These discussions have not yet been concluded for the most part, which does not allow all these trials to start yet. By the end of 2022, only GSK had responded favourably and agreed to supply dostarlimab (anti-PD1) and allowed the initiation of the MSI cohort. The AcSé-Pan MSI trial is expected to start in 2023. Discussions are on-going and other cohorts may be set up in the coming years.

Clinical cancer research organisation: structures, infrastructures, and tools

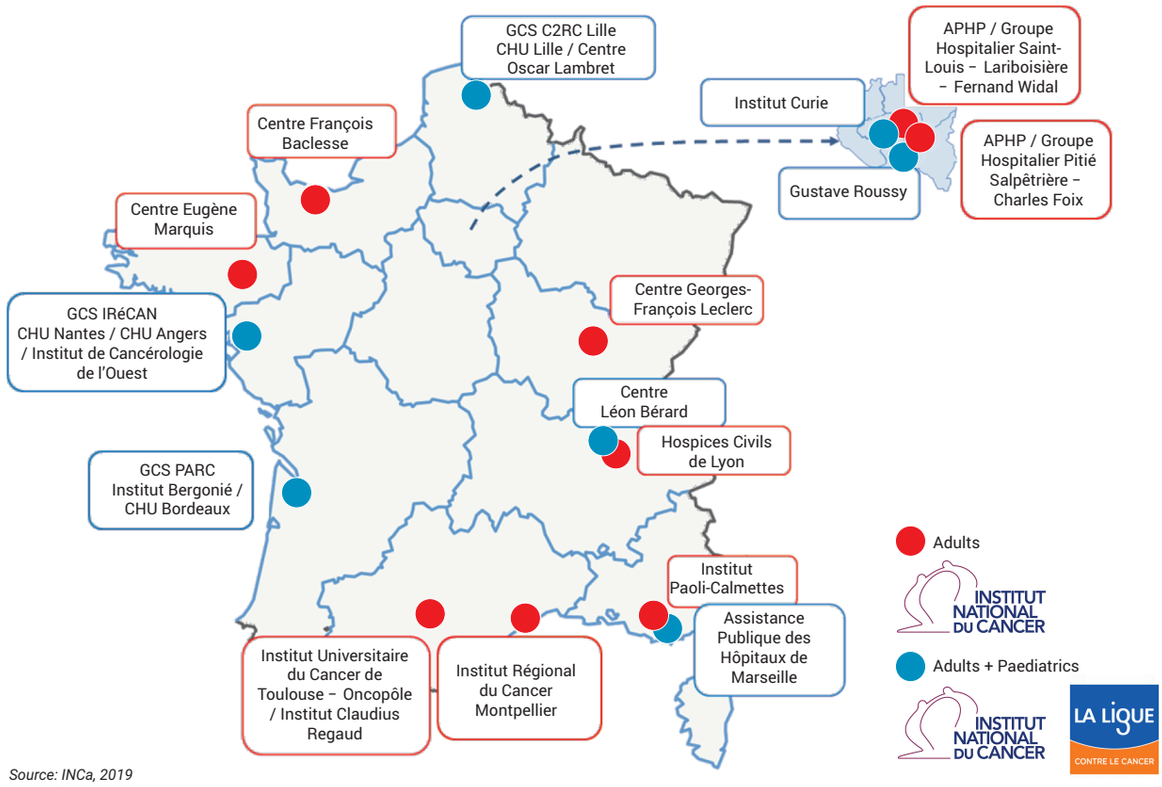
CLIP² – EARLY-PHASE CLINICAL TRIAL CENTRES

Sponsored by the 2009-2013 Cancer Control Plan, the initiative to structure clinical and translational research is supported by INCa through a specific designation: early-phase clinical trial centres known as CLIP² centres (Centres Labellisés de Phase Précoce). The second 2009-2013 Cancer Control Plan allowed the French National Cancer Institute to launch the set-up of specialised investigation centres in early-phase clinical trials. Thanks to the first designation initiated in 2010, the Institute has provided CLIP² centres with logistical and financial support

in order to reach the highest international level in terms of quality, in carrying out early-phase clinical trials evaluating new drugs from pharmaceutical firms, biotech companies, or academic research.

This objective was continued in the 2014-2019 Cancer Control Plan by conducting, in partnership with the French Cancer League, a new designation of these structures in 2015, and identifying centres with paediatric activities. The third and latest designation has made it possible to renew and bolster its support for expert centres in early-phase clinical trials for adult and paediatric, adolescent and young adult cancers. Thus, among the 16 structures designated until 2024, seven include paediatric oncology activities (Figure 36).

FIGURE 19
GEOGRAPHIC DISTRIBUTION OF CLIP² CENTRES (3RD DESIGNATION – 2019-2024)



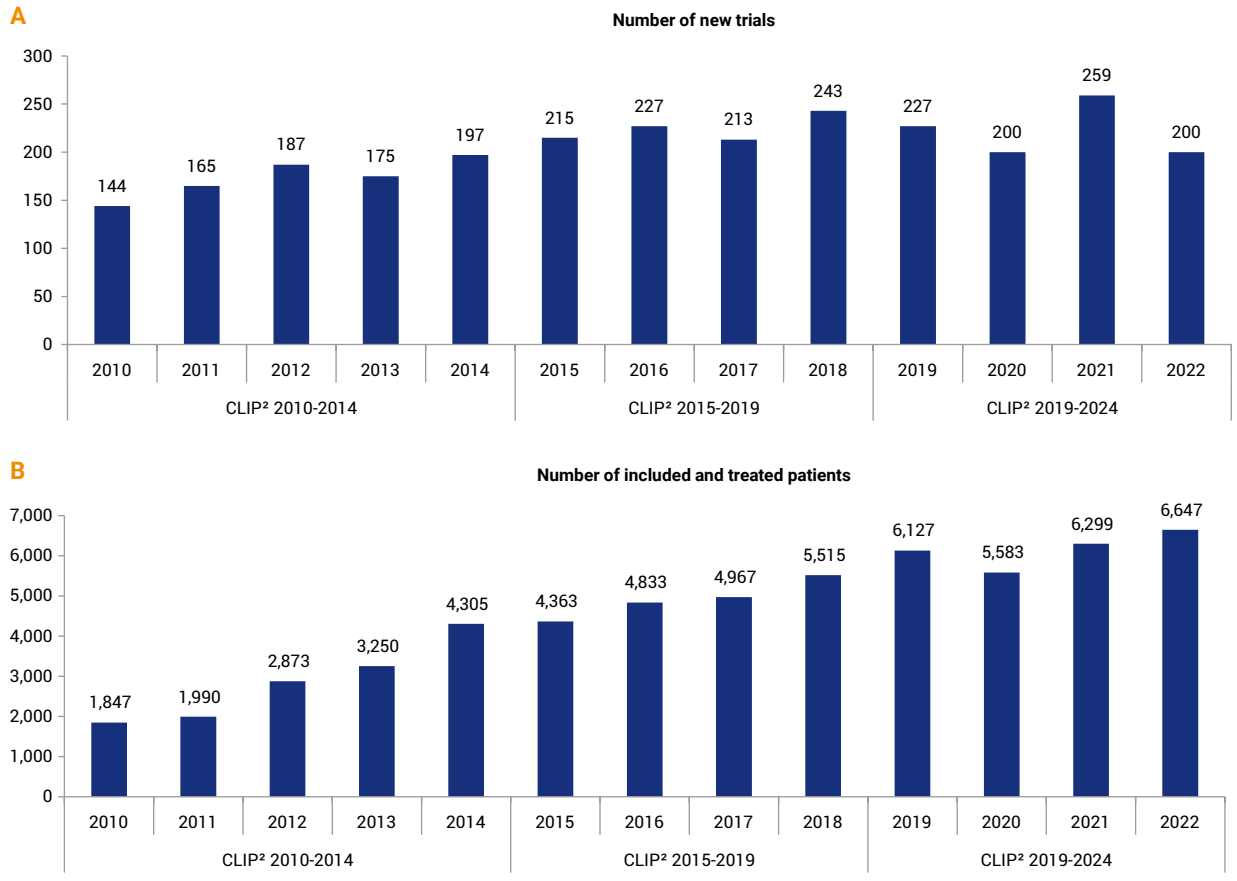
Source: INCa, 2019
Drafted by INCa's Research Division, 2020

This programme has helped increase the visibility and attractiveness of these centres and also those of early-phase French clinical research (and should continue to do so), leading not only to an increase in the number of new trials launched, and in the number of patients included every year within CLIP², but also to a growing interest of pharmaceutical companies in conducting early-phase clinical trials within these designated centres.

Since 2010 (i.e. the first designation campaign), this initiative has contributed to the overall increase in the number of clinical trials initiated and the number of patients enrolled in CLIP² centres (Figure 20):

- + 40% increase in the total number of clinical trials launched, with 200 in 2022, despite an apparent decrease of 25% between 2021 and 2022;
- + 259% increase in the total number of patients enrolled, with 6,647 patients enrolled and treated in 2022.

FIGURE 20
TRENDS IN PROGRESSION OF THE NUMBER OF TRIALS INITIATED (PANEL A) AND PATIENTS ENROLLED (PANEL B) OVER THE 2010-2022 PERIOD



Bibliographic report on social inequalities in health and early-phase cancer clinical trials (Measure IV.3.7: "Make sure that vulnerable populations are included in clinical trials.")

Because of their personal vulnerability (disability, advanced age, language difficulties, etc.), their socio-professional status (CSP) or their particular circumstances (prison detention), some people find it difficult to access a quality healthcare pathway, including access to clinical trials. As part of action IV.3[1] of the France ten-year cancer-control strategy (2021-2030), which focuses on the fight against inequalities in access, measure IV.3.7[2] aims to include these vulnerable populations in clinical trials.

It is in this context that Sylvain Besle, sociologist with the SINCRO Group on care trajectories in cancer care[3] and holder of the SHS-INCa chair[4], was asked by the Institute, to identify the obstacles and tools associated with these inequalities of access and to draw up a bibliographic summary on the role of these vulnerable populations in clinical trials, with initial recommendations and investigation avenues.

Among these tools, the setting up of a prospective study aiming to assess social inequalities in the health of patients included in early-phase clinical trials within CLIP[2] centres was one of the objectified actions.

In 2022, INCa therefore decided to support and fund the implementation of this study, for which the operational set-up within CLIP[2]s is scheduled for 2023.

[1] Action IV.3: Combatting inequalities through a pragmatic approach tailored to various populations
[2] Mesure IV.3.7 : Veiller à inclure les populations vulnérables dans la conduite d'essais cliniques.
[3] Working group resulting from the collaboration of researchers from SESSTIM (Health Economic and Social Sciences and Medical Information Processing, Marseille) and Gustave Roussy (Villejuif)
[4] https://www.e-cancer.fr/Actualites-et-evenements/Actualites/Creation-d-une-chaire-de-recherche-en-SHS-appliquee-au-cancer

COOPERATIVE INTERGROUPS

2022 designation:

The French cancer cooperative intergroups are independent and not-for-profit academic groups, bringing together doctors and medical research professionals who collaborate to develop and conduct clinical trials.

The aims of the designation of cooperative intergroups are to:
- promote grouping and improve collaboration between cooperative groups at a national level and cover different cancers;
- promote interaction between INCa and cooperative groups in carrying out clinical trials and translational research, and help boost clinical research in France;
- improve the international visibility and attractiveness of clinical research in France, and to develop European and international cooperation in clinical and translational research in France.

INCa has designated cooperative intergroups since 2012. The last designation campaign took place in 2022.

This campaign has resulted in the designation of 14 intergroups; this designation will end in December 2027. The annual amount of allocated funds is €50K, mostly earmarked to help structure the intergroups.

Their involvement is anticipated in the participation of the Ten-year cancer control strategy against cancer, particularly in clinical trials aimed at major therapeutic challenges, *i.e.* increasing survival, reducing treatment side-effects and delayed effects particularly by setting up de-escalation trials.

TABLE 22
LIST OF COOPERATIVE INTERGROUPS DESIGNATED IN 2022

Cooperative intergroup	Diseases covered
ARCAGY-GINECO	Gynaecological cancers
CIGAL	Acute leukaemia
DIALOG	Geriatric oncology
GETUG-AFU Alliance	Urological cancers
GRRR-OH	Intensive care unit – all cancers
IFCT	Thoracic cancers
IGCNO	Neuro-oncology
IFM	Myeloma
Intergroupe ORL	ENT cancers
INTERSARC	Sarcomas
LYSA-LYSARC	Lymphomas
PRODIGE	Digestive cancers
SFCE	Paediatric oncology
UCBG	Breast cancers

Since 2020, a declarative survey on clinical cancer research activity has been specifically designed at the request of the cooperative intergroups and based on the national survey (see section 3.4.3 Enrolments of patients in clinical trials). This survey is aimed at quantitatively assessing clinical cancer research activities in France in these cooperative intergroups every year.

As a reminder, cooperative intergroups may be sponsors, and may be involved in academic trials, and/or industrial trials: these three statuses have been addressed[3].

Table 23 presents the main results of the survey conducted in 2022:

- in 2021, 107 cancer clinical trials were sponsored by 11 cooperative intergroups (or a group of the intergroup):
  - 25,910 inclusions were reported in 2,098 French centres (+ 152% increase compared to 2020),
  - these 11 cooperative intergroups, as sponsors, were active at an international level with 106 participating centres abroad;
- all the cooperative intergroups were involved in academic trials with 198 cancer clinical trials reported and 11,803 inclusions. A 22% increase in the number of inclusions in 2021 was reported compared to 2020;
  - five cooperative intergroups were involved in industrial trials with 33 clinical cancer trials and approximately 311 inclusions reported,

3. Members of the cooperative intergroups participate in the design of the study methodology and/or the inclusion and follow-up of patients in the study.

- with a total of 38,024 inclusions in 2021, they represented 66% of national inclusions. The total number of inclusions in 2021 increased compared to 2020 (20,346 inclusions reported in 2020),
- strong clinical research activity in early phases (phase 1 and 1/2) and phase 3 was still observed in 2021,
- 92% of inclusions were observed in phase 3 when the cooperative intergroups were sponsors,
- 10% of inclusions were observed in early phases when the cooperative intergroups were involved in industrial trials.

Moreover, this survey analysed the staff involved in clinical cancer research activities: 172 members of clinical research staff (full-time equivalent) were assigned to clinical cancer research in cooperative intergroups in 2021.

These results highlight the key role of intergroups in the clinical cancer research landscape, particularly in academic trials, both in terms of the design and conduct of clinical trials.

TABLE 23
MAIN RESULTS OF 2021 CLINICAL CANCER RESEARCH ACTIVITY AMONG COOPERATIVE INTERGROUPS

Status of cooperative intergroup	Number of cooperative intergroups			Number of trials			Number of inclusions		
	2019	2020	2021	2019	2020	2021	2019	2020	2021
Sponsors	9	11	11	86	100	152	7,192	10,272	25,910
Involvement in academic trials	13	13	13	162	198	198	12,469	9,652	11,803
Involvement in industrial trials	7	6	5	39	36	33	714	422	311

ENROLMENT OF PATIENTS IN CLINICAL TRIALS

Within the framework of Area III.5 "Ensuring access for patients to innovative therapies within the scope of clinical trials" of the 2021-2030 Cancer Control Strategy, INCa's annual declarative survey assesses clinical cancer research activities in France. Using the data reported by University Hospitals, Cancer Care Centres, and Public and private Health Care Centres, this survey provides an estimation of the enrolment rate in cancer clinical trials every year in France. These data are presented annually to the French President.

In 2021, 57,644 patients were included in a clinical trial (Table 24):
- 34,235 patients in a therapeutic clinical trial;
- 82% were enrolled in academic trials;
- 43,616 patients in clinical trials addressing solid tumours;
- 7,185 in haematology.

Childhood and adolescent cancers are a priority of the 2021-2030 Cancer Control Strategy:

- 1,940 inclusions concerned children in 2021, with 95% included in academic trials;
- 1,528 inclusions concerned adolescents and young adults, with 89% enrolled in academic trials.

Another indicator closely monitored by the Cancer Control Strategy is the inclusion of elderly subjects. In 2021, 3,852 inclusions concerned patients over 75 years of age in total, 88% of these included in academic trials.

TABLE 24
MAIN RESULTS OF CLINICAL CANCER RESEARCH ACTIVITY SURVEY IN 2021

	Academic	Industrial	TOTAL 2021
Number of inclusions	47,075	10,569	57,644
Number of inclusions in therapeutic clinicaltrials	24,481	9,754	34,235
Number of inclusions in clinical trials in solid tumours	35,324	8,292	43,616
Number of inclusions in clinical trials in haematology	6,001	1,184	7,185
Number of inclusions of children (0-18)	1,838	102	1,940
Number of adolescent and young adult inclusions (15-25)	1,361	166	1,528
Number of elderly adult (≥ 75 years old) inclusions	3,400	452	3,852

The results of INCa's annual survey in 2021 show a steady increase in the number of patients enrolled in clinical trials for the last 13 years:

- over the 2009-2021 period, the number of patients enrolled in cancer clinical trials more than doubled, probably due to the actions of the different Cancer Control Plans (Figure 21);
- the ratio of enrolment in academic versus industrial trials remained stable over the years, with a significant majority of inclusions in academic trials (76% versus 24%). However, between 2009 and 2021, greater growth was observed in academic trials (+ 121%) than in industrial trials (+ 67%) (Figure 21);
- there was a 17% increase in the number of patients enrolled in therapeutic trials in 2021 compared to 2020, with 34,235 patients included in therapeutic cancer clinical trials in 2021. The ratio of therapeutic trials grew significantly from 51.8% to 62.6% between 2017 and 2019 and decreased slightly by 14% in 2021 (Figure 22);

FIGURE 21
GROWTH OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS (2009-2021)

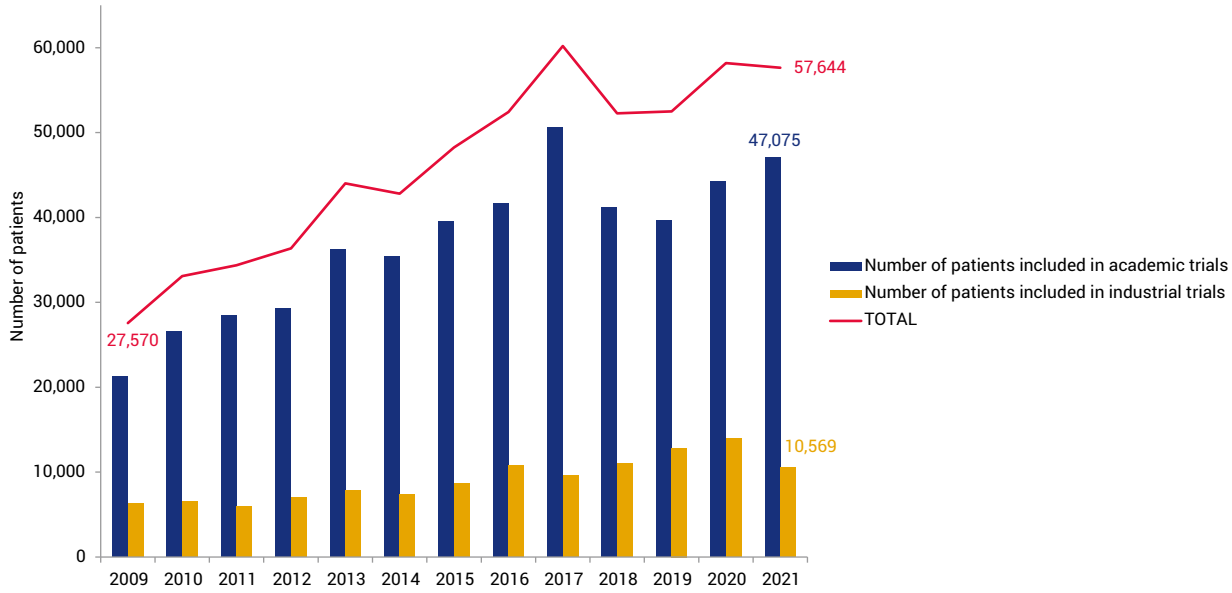
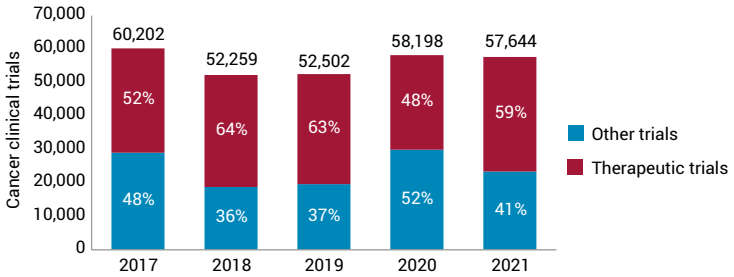


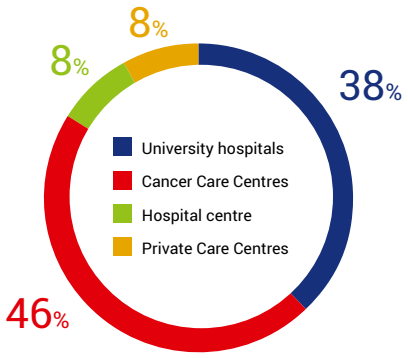
FIGURE 22
DISTRIBUTION OF CANCER CLINICAL TRIALS ACCORDING TO THERAPY OVER THE 2017-2021 PERIOD



- the distribution among the different care providers was quite similar over the years: in 2021, 38% of the patients were enrolled in University Hospitals, 46% in Cancer Care Centres, and 8% in Public and Private Health Care Centres, respectively (Figure 23);

2021: 57,644 patients recruited in cancer clinical trials, including 34,235 in therapeutic trials
- 43,616 patients in clinical trials in solid tumours and 7,185 trials in haematology
- 1,940 children enrolled
- 1,528 adolescents and young adults enrolled
- 3,852 patients are over 75 years
- 1,641 clinical research staff assigned to clinical cancer research.

FIGURE 23
DISTRIBUTION OF PATIENTS ENROLLED IN CANCER CLINICAL TRIALS AMONG DIFFERENT CARE PROVIDERS IN 2021



- one of the objectives of the 2021-2030 cancer control strategy is to open investigating centres in the French overseas territories to increase trial inclusions (action 5.2). In 2021, the University hospitals CHU Martinique, CHU Guadeloupe and CHU La Réunion included 312 patients in academic cancer clinical trials;
- furthermore, this survey analysed the staff involved in clinical cancer research activities. The results show that 1,641 members of clinical research staff (full-time equivalent) were assigned to clinical cancer research in 2021 with 46% concentrated in University Hospitals. Over the 2009-2021 period, there was a constant increase in the number of clinical cancer research staff (+151% between 2009 and 2021).

INCA'S CANCER CLINICAL TRIALS REGISTRY

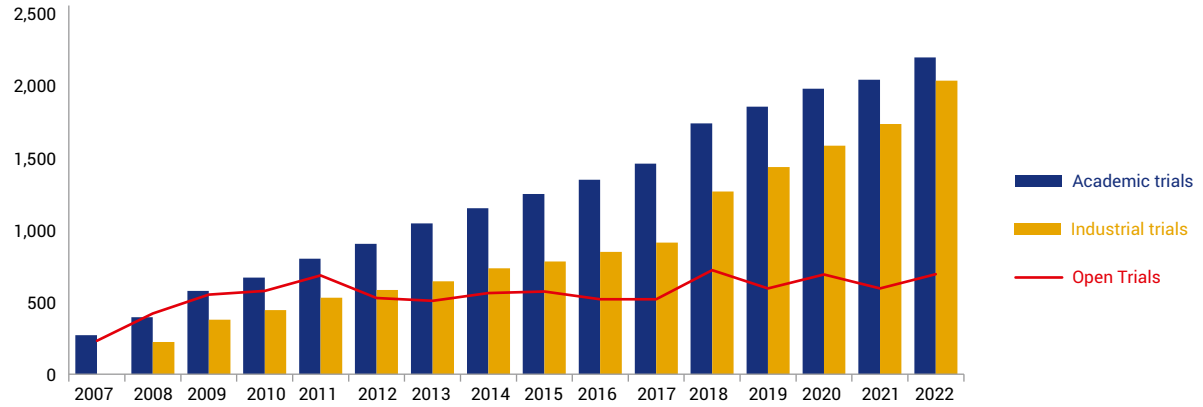
Since 2007, INCa's cancer clinical trials registry has allowed easy access to cancer clinical trials conducted in France. It is freely accessible on INCa's website, and enables provision of quality and regularly updated information to patients, health professionals and the general public.

The INCa cancer clinical trials registry provides information accessible to the general public, and facilitates the search and selection of clinical trials. Visitors to the clinical trials registry can, with the help of a multicriteria search engine, accurately target their search using different selection criteria, such as the sponsor or target organ, and can also apply the geographic criterion using the geolocation module included in the registry.

TABLE 25
INCA'S CANCER CLINICAL TRIALS REGISTRY

Objectives	Provide information on cancer clinical trials conducted in France.
Results	4,236 clinical trials advertised on INCa's website in December 2021, sponsored by more than 508 industrial and academic bodies. 693 on-going recruiting trials: • 50 % are sponsored by academic bodies. • 80 % of treatment trials.

FIGURE 24
NUMBER OF CLINICAL TRIALS IN THE REGISTRY PER YEAR (DECEMBER 2021)



Focus

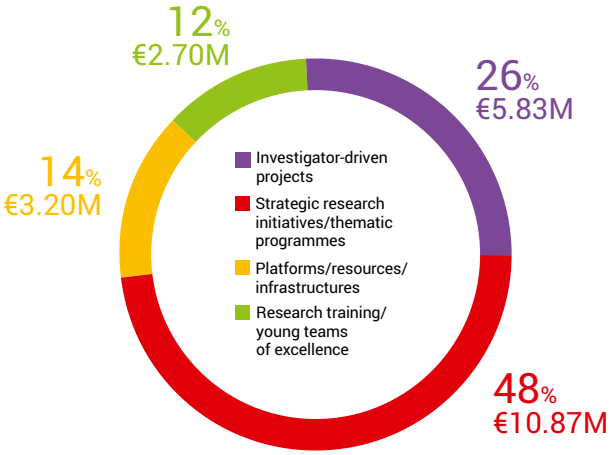
INCa has developed a new database for the registration and the administration of clinical trials. This new portal has been accessible since December 2022 online for academic and industrial sponsors of cancer clinical trials in order to register their trials directly in the webpage of the new database. Users have already started entering their clinical trials data and documents.

RESEARCH IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH

One of INCa's goals is to bring human and social sciences, epidemiology, and public health research on cancer in France up to the best international standards. Particular efforts are being devoted to increasing basic and health intervention research. Specific emphasis is placed on reducing social inequalities related to cancer, as well as increasing the impact of cancer prevention measures, participation rates in national screening programmes, and access to care.

In 2022, support for human and social sciences, epidemiology and public health amounted to:

€22.61M



Merged research programme for human and social sciences, epidemiology, and public health applied to cancer and population health intervention research

The contributions of public health (PH), human and social sciences (HSS) and population health intervention research (PHIR) in the fight against cancer are significant. They cover a multitude of fields of research in which the non-medical perspective is proving to be increasingly relevant. Questions remain about social perceptions of cancer, barriers to screening, environmental factors, and health risk behaviours.

The objectives of HSS research are to contribute to a better understanding of the determinants of health, prevention and the impact of cancer on the lives of those affected and their families, and to improve the entire care pathway, in particular by encouraging and supporting multidisciplinary approaches. PHIR, also defined as the science of "solutions", designs intervention hypotheses, innovative and effective support systems for and with all stakeholders (field workers, populations, patients and their families, healthcare professionals, decision-makers, researchers, etc.), their implementation and transferability.

In 2022, a merged HSS and PHIR research programme was launched, organised around four areas:

- two unrestricted sections (one HSS and the other PHIR) based on the two historical calls for proposals: the call for proposals in human and social sciences, epidemiology and public health (HSS-E-PH) launched in 2007, and the call for proposals in population health intervention research (PHIR) launched in 2010;
- two thematic sections (on HSS and the other PHIR) that meet the objectives of the Ten-year cancer strategy. These thematic sections integrate three research priorities:
  - combatting inequalities through a pragmatic approach tailored to different populations,
  - taking action to reduce cancer in children, adolescents and young adults,
  - developing research in cancers with a poor prognosis.

In 2022, 23 projects were selected from the 58 submitted for total funding of €7.05M (Table 26).

International scientific conference on "cancer, work & employment"

In Europe, more than two million working-aged people are diagnosed with cancer each year. The impact on both personal and work lives encountered during the disease forms barriers to accessing, resuming or maintaining professional activity.

Faced with this issue, INCa organised an international scientific conference on 21-22 November 2022, in Paris, on "Cancer, Work & Employment", to discuss current challenges in Europe and outline further research perspectives. Giving an unprecedented specific focus on this theme, it was attended by more than 110 researchers from 22 countries.

This conference welcomed more than 50 scientific communications in four main areas:

- Overview of the situation
- Legislation
- Return and access to work, job retention and impact of cancer on work
- Diversity of occupational trajectories.

TABLE 26
FEATURES OF THE HSS AND PHIR PROGRAMME IN 2022

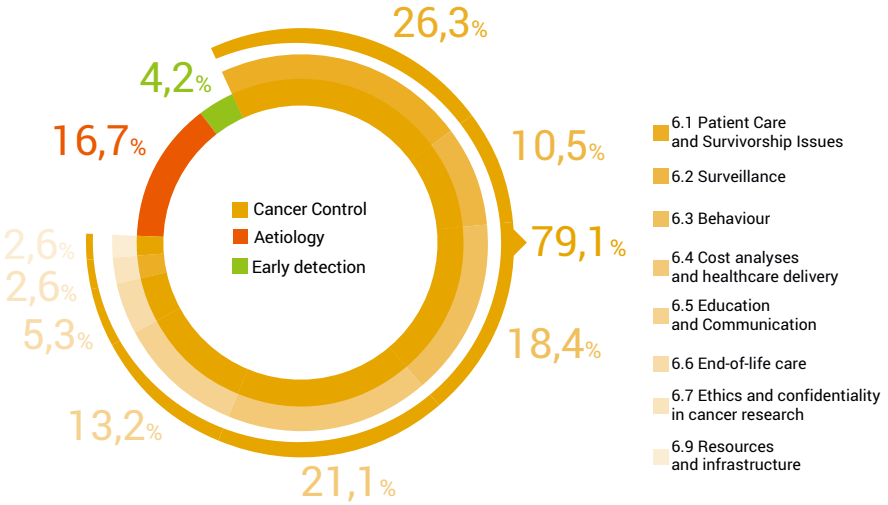
Objectives	• To enable the development and emergence of original research projects applied to cancer, and to encourage the production of new knowledge guaranteeing its scientific validity; • Opening up new perspectives in our understanding of cancer-related issues and practices; • Promoting and encouraging the decompartmentalisation of research disciplines; • Encouraging and supporting projects that aim to co-construct an intervention/solution, particularly for patients and their families, with a favourable impact on all health determinants.
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	**€7.05M**
Proposals submitted	**Total = 58 (47 in HSS and 11 in PHIR)**
Projects selected	**Total = 23 (23 in HSS and 8 in PHIR)**
Unrestricted section	*Total = 15 (9 in HSS and 6 in PHIR)*
Thematic section	*Total = 8 (6 in HSS and 2 in PHIR)*
Selection rate	**39.6%**

15 funded projects were selected in the unrestricted section, focusing on the following subjects in particular: personalised care pathways and accessibility, screening, return to work, supportive care and the impact of adapted physical activity, post-cancer, co-morbidities, social inequalities in health, and risk factors and environments.

8 funded projects were selected in the thematic section, including 1 on cancers with a poor prognosis, 4 on the fight against inequalities, and 3 on cancers in children, adolescents and young adults.

Figure 25 shows the distribution of funded projects according to the CSO classification. The 'cancer control' category is the largest: 79.2% of funded projects, with more than half of these projects focusing on patient management and survival (26.3%), cost analysis and healthcare provision (21.1%), and behaviour (18.4%).

FIGURE 25
DISTRIBUTION OF PROJECTS SELECTED FOR FUNDING IN THE HSS AND PHIR PROGRAMME IN 2022, ACCORDING TO THE CSO CLASSIFICATION



Webinar: "Population health intervention research, a tool in the Ten-year cancer control strategy"

This webinar was organised in September 2022 in consultation with and for the scientific community. It responds to a need in this community to discuss cross-cutting PHIR themes.

The webinar focused on the contribution of PHIR to the implementation of the ten-year cancer control strategy. Firstly, the 8 new projects funded under the 2022 PHIR call for proposals were presented. This was followed by a round-table discussion on innovative research tools and their contribution to the ten-year strategy (research chairs, primary prevention research networks). This webinar was attended by 80 participants and 13 speakers.

Research programme on primary prevention and health promotion

Even though some cancer risk factors are now well-documented, additional research is needed to: develop innovative intervention models, understand exposure to presumed cancer risk factors, and implement favourable environments tackling health determinants.

In line with these challenges, INCa's Ten-Year Cancer Control Strategy supports research to help build public health action plans. In 2022, it launched a dedicated call for proposals addressing "Primary Prevention & Health Promotion" within the programme of Human & Social Sciences, Epidemiology, Public Health (HSS-E-PH) and Intervention Research. This programme was aimed at:

- developing knowledge of risk factors and ways to reduce exposure;
- identifying determinants and favourable environments for health;
- increasing knowledge of intervention models, design, evaluation, transferability, and implementation for the development of health-promoting behaviours.

9 projects were selected for a total amount of €2.8M:

- 6 in PHIR covering health promotion and health literacy for vulnerable populations, young people and in school settings;
- 3 in HSS-E-PH covering the understanding of cancer risks linked to a sedentary lifestyle, green space exposure, and analysing health perceptions.

Programme to support research networks in primary cancer prevention and health promotion

Primary prevention in France appears to be segmented, interweaved with different approaches, and poorly developed regarding its expected benefits for public health. Improving cancer prevention is one of the priorities of INCa's Ten-Year Cancer Control Strategy and to face these challenges, in 2021, it launched a structuring research call for applications to:

- increase research skills in this field;
- establish partnerships and strengthen collaborations;
- develop research questions and innovative scientific projects.

Selected by an international scientific committee in 2022, two multidisciplinary research networks were funded:

CANCEPT, Cancer Primary Prevention Transdisciplinary Nutrition and Environment Research Network, a multidisciplinary approach to identify nutritional and environmental cancer risks factors, their interactions, and ways to implement this knowledge in effective prevention;

SoRISP, Research Network for the Expansion of PHIR, to develop knowledge, skills, expertise, tools and training in population health intervention research to identify and document effective, efficient and socially acceptable interventions in cancer prevention.

These networks have been funded for four years with €1.6M each. A mid-term follow-up seminar of their research programme will be organised in 2024.

CPE – Cancer Prevention Europe

Cancer Prevention Europe (CPE), a consortium of organisations across the whole of Europe, aims to reduce morbidity and mortality from cancer in European populations through prevention and earlier diagnosis of the disease. This consortium is coordinated by the International Agency for Research on Cancer, (IARC) and is composed of several members (Cancer Research UK, Danish Cancer Society, European Institute of Oncology, the French National Cancer Institute, German Cancer Research Center, UK Therapeutic Cancer Prevention Network, Imperial College London, Karolinska Institut, Maastricht University, World Cancer Research Fund International and IARC). One of the missions of CPE is to support cancer prevention research strategies with the aim of benefiting from shared research capacities and coordinated perspectives for public health translation. The CPE Steering Group have called for dedicated meetings to develop a "Cancer Prevention Research Roadmap" in order to advocate for increased investment in the area by highlighting current priorities. It was the main action of this year.

Supporting research addressing psychoactive substance abuse and addiction

Tobacco and alcohol are the leading causes of avoidable death in France. Tobacco consumption is responsible for 75,000 deaths per year, including 45,000 deaths from cancer; alcohol is responsible for 41,000 deaths, including 16,000 deaths from cancer[4].

In order to fund tobacco control actions, a specific fund was set up in December 2016 within the French National Health Insurance Fund (CNAM) and is notably financed by a tax on tobacco products. In 2019, the scope of intervention of this fund was extended to all psychoactive substances and became the Addictions Fund.

4. Observatoire français des drogues et des toxicomanies – https://www.ofdt.fr/BDD/publications/docs/DACC-2022.pdf

The governance of the fund is based on a Strategic Orientation Council (COS) chaired by the Director General of the National Health Insurance Fund and is composed of representatives of the National Health Insurance Fund associations involved in combatting addiction, public agencies or organisations in the field of health; administrations in the fields of health, research, education and justice.

This fund aims to perpetuate existing addiction control and prevention initiatives; it is also an opportunity to propose funding of new initiatives, particularly for supporting research actions.

In 2022, the Addictions Fund allocated €16M to INCa and the Institute for Public Health Research (IReSP) to deploy research and intervention measures against addiction.

PSYCHOACTIVE SUBSTANCES PROGRAMME

In the context of the Addictions Fund, INCa and IReSP are jointly in charge of a call for proposals to combat psychoactive substance use and addiction. This programme follows on from the "Tobacco INCa-IReSP" programme that was implemented in 2018 and 2019 and whose scope has been extended to all psychoactive substances.

This call for proposals aims to support research and to produce knowledge in the field of psychoactive substance use and the fight against addiction, in priority in relation to tobacco, alcohol and cannabis, identified as proven risk factors for cancer, but also in relation to other psychoactive substances as well as in relation to polysubstance use. It covers a wide range of disciplines, from intervention research, through to human and social sciences, economics and political sciences, law, psychiatry, information and communication technologies, epidemiology, addiction studies and other public health disciplines.

This call for proposals is open to researchers as well as to health or other professionals who wish to engage in a research process. The teams can therefore be composed of researchers, health professionals, health prevention and health promotion professionals, user associations and decision-makers.

It is divided into 3 sections:
- section 1 (INCa-IReSP): Psychoactive substances and the general population;
- section 2 (INCa): Psychoactive substances and cancer;
- section 3 (IReSP): Psychoactive substances and diseases other than cancer.

Candidates can submit three types of proposals:
- "full research proposals" (36 to 48 months – minimum budget of €100,000/project): projects that are advanced in their design and that are based on a controlled methodological approach and successful collaborations based, in particular, on data from pilot studies, emerging projects or feasibility assessments;

- "pilot proposals" (18 to 24 months – maximum budget of €100,000/project): small-scale preliminary studies to determine the feasibility, time, cost and risks before conducting a similar project on a larger scale;
- "emerging proposals" (12 to 18 months – maximum budget of €50,000/project): proposals aimed at developing research questions and intervention designs. This seed funding allows researchers to build a proposal that will be submitted (as a pilot proposal or a full proposal) to the next round of the call.

TABLE 27
FEATURES OF THE PSYCHOACTIVE SUBSTANCES PROGRAMME IN 2022 (SECTIONS 1 & 2)

Objectives	To support research and to produce knowledge in the field of psychoactive substance use and the fight against addiction
Programming institution	INCa and IReSP
Operating institution	INCa and IReSP
Funding institution	INCa and IReSP
Funding	**€7,11M** **INCa: €4,29M** **IReSP: €2,82M**
Proposals submitted	**44**
Projects selected	**23**
Selection rate	**52%**

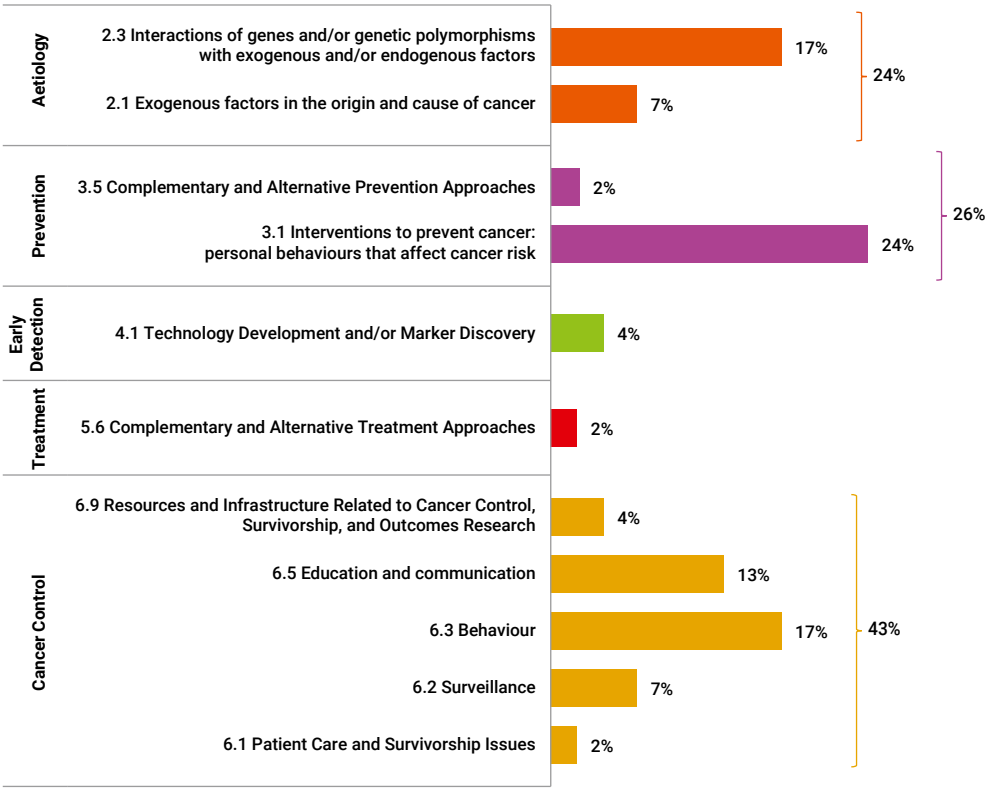
INCa-NCI workshop – Current state of Tobacco Cessation Interventions & Tobacco Prevention Research

INCa co-organised a workshop with the National Cancer Institut (NCI) on the "Current State of Tobacco Cessation Interventions and Tobacco Prevention Research", as part of an institutional and scientific partnership established in 2019.

This workshop took place in November 2022 at INCa and brought together nearly 50 (American and European) researchers and experts in the field of tobacco. A virtual pre-meeting was held in February 2022 to present a whitepaper summarising a review of the American and European literature on the subject, and to provide an initial opportunity for researchers to meet.

The aim of the workshop was to review the knowledge that has been acquired (what we know?), identify gaps (what we don't know?) and ways of filling these gaps (how to fill them?) in 3 areas: 1/ Tobacco use and co-behaviours; 2/ Multiple tobacco product use; 3/ Health disparity, Hard-to-reach populations. A scientific roadmap identifying research priorities (what themes and what tools should be used to structure research in this field?) is currently being drawn up and will be presented in 2024. This event was financed by the Addictions Fund, managed by Caisse Nationale de l'Assurance Maladie (CNAM).

FIGURE 26
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PSYCHOACTIVE SUBSTANCES PROGRAMME IN 2022 (SECTIONS 1 &2)



International Scientific Conference on E-Cigarettes

The E-Cigarette appeared on the Asian market in 2000 and in Europe in 2010. The scientific literature on this new tobacco product has grown significantly since 2016, with an over-representation of American studies and results that have yet to be consolidated.

In this scientific context, an international scientific conference on E-Cigarettes was held in December 2022 in Paris. Its aim was to create a special meeting place for international researchers and experts on this topic, and to review on-going research and identify any outstanding research questions by focusing on two central areas: health effects and patterns of use.

Over 200 people of 31 different nationalities attended the conference. More than 50 speakers presented their work in oral sessions, posters or symposia. Several scientific articles will be published in 2024 to promote this conference. This event was financed by the Addictions Fund, managed by the French National Health Insurance Fund (CNAM).

In this second year of the call including all psychoactive substances, more than half of the projects funded (13) in section 1 and 2 are studying several psychoactive substances, notably in polysubstance use. The majority involve at least tobacco (7 projects), alcohol (8 projects) and/or cannabis (6 projects). The remaining funded projects are focusing on addiction mechanisms and other substances. Also, nearly 40% of projects are enlisting and linking several disciplinary approaches, which is strongly promoted by the Institute.

- Projects funded in Section 1 address diverse multidisciplinary research themes such as addiction mechanisms, treatment of substance use disorders, consumption pathways and risk factors for addiction.
- A total of 4 projects were funded in Section 2 (psychoactive substances and cancer), including 1 emerging project and 3 full projects. These projects address addiction in cancer patients or survivors and the link between substance use and cancer.

PSYCHOACTIVE SUBSTANCES PHD PROGRAMME

INCa's support for research addressing psychoactive substances use and addiction includes a dedicated PhD call for applications. Based on the same model as the call for proposals, the call for applications for PhD grants is managed jointly with the Institute for Public Health Research (IReSP) and is open to all psychoactive substances and is divided in three sections:

- section 1 (INCa-IReSP): Psychoactive substances and the general population;
- section 2 (INCa): Psychoactive substances and cancer;
- section 3 (IReSP): Psychoactive substances and diseases other than cancer.

The programme covers all aspects of research, as well as a broad array of disciplines, ranging from clinical research to public health, and including information and communication technologies, economics and political science, human and social sciences, law, biology, and epidemiology.

Aimed to support PhD students with a 3-year grant, this call for applications targets all students with a Master's degree in human and social sciences, public health, epidemiology, or biology, enrolled in first or second year in a doctoral school.

In 2022, 23 applications were submitted (13 in neurosciences, 7 in human and social sciences, 3 in public health and epidemiology).

9 PhD students were selected and are funded by INCa (4 applicants) and IReSP (5 applicants). The 4 PhD thesis projects funded by INCa concern:

- cannabinoids and germ cell tumours of the testis;
- determinants of alcohol and tobacco withdrawal in the case of upper aero-digestive tract cancers: what lessons can we learn for future care?;
- preventing addiction and risk behaviour among young people at risk of social exclusion;
- epigenetic biomarkers of opioids: a translational study in mice and humans.

Lung cancer: perspectives on prevention research

Lung cancer is responsible for 46,300 new cases of cancer each year in France. It is the leading cause of cancer death (33,100 deaths), accounting for around 20% of all cancer deaths, and smoking is the main risk factor. It is also a cancer with a poor prognosis, with a 5-year survival rate of 20%. Since February 2022, INCa has been coordinating a pilot programme for organised lung cancer screening.

In this context, a scientific conference on lung cancer was organised in October 2022. Its aim was to mobilise the scientific community by disseminating the knowledge produced to date on this topic, to promote the projects funded by INCa and, in particular, to discuss the contribution of human and social sciences to this research. The conference brought together nearly 80 participants and 15 speakers. This event was financed by the Addictions Fund, managed by CNAM, the French National Health Insurance Fund .

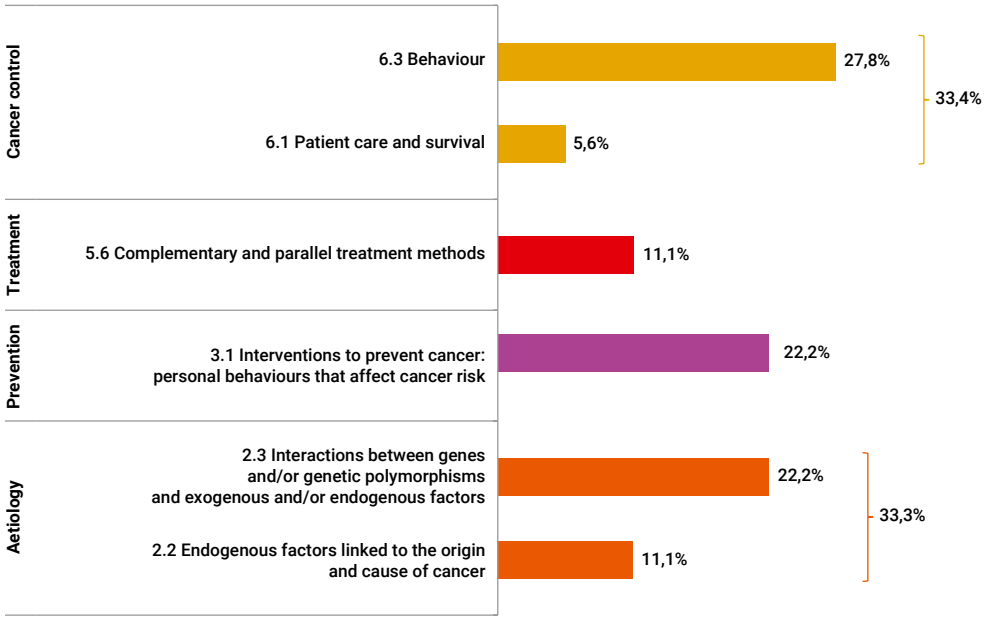
TABLE 28
FEATURES OF THE PSYCHOACTIVE SUBSTANCES PHD PROGRAMME IN 2022

Objectives	To support PhD research and to produce knowledge in the field of psychoactive substance use and the fight against addictions
Programming institution	INCa and IReSP
Operating institution	INCa and IReSP
Funding institution	INCa and IReSP
Funding	**€1.15M**
Proposals submitted	**23**
Projects selected	**9**
Selection rate	**39%**

The majority of the theses funded were in section 1 (6 out of 9). The main themes were addiction prevention among socially vulnerable young people, and smoking and alcohol cessation.

This is the third year that the call has been opened to all psychoactive substances, and 4 out of 9 theses focused exclusively on cannabis, which shows the attractiveness of this topic.

FIGURE 27
DISTRIBUTION OF FUNDED PROJECTS FOR THE PSYCHOACTIVE SUBSTANCES PHD PROGRAMME IN 2022, ACCORDING TO THE CSO CLASSIFICATION



PROGRAMME FOR JUNIOR RESEARCHERS IN TOBACCO AND/OR ALCOHOL

In 2020, INCa launched an innovative programme aimed at junior researchers who have defended a PhD thesis in the last ten years, and are interested in tobacco and/or alcohol research, and would like to propose innovative ideas in the field of research in human and social sciences, public health and intervention research on these themes, in order to reduce the risks of cancers associated with these psychoactive substances.

The objective of this programme is to attract young PhD researchers to participate in the development of tobacco and/or alcohol research, by proposing new models, approaches, methodologies and scientific protocols.

The aim is both to support research on tobacco and/or alcohol through a collaborative system of initiatives led by junior researchers, and furthermore to develop a scientific community around these themes.

This call for applications is organised in three phases:
- pre-selection of candidates based on letters of intent;
- development of projects including participation in a collaborative seminar;
- selection of candidates based on projects and interviews.

The programme in 2022

In 2022, 18 eligible applications were submitted and 13 were pre-selected based on letters of intent for the second stage of the call. Half of the applications submitted (9) were projects relating to population health intervention research, which underpins the fact that junior researchers are inclined to invest in this type of research that the Institute is seeking to foster.

The distribution of projects submitted according to the substance studied is balanced between tobacco and alcohol (7 projects on tobacco, 8 on alcohol, and 3 dealing with both substances).

9 junior researchers were selected for funding and their projects concern:
- economic evaluation and budgetary impact of a financial incentive to stop smoking during pregnancy;
- history of the French Anti-Alcohol Movement – MALCOF database;
- development of Smoking Cessation Strategies Among Migrants, a Participatory Approach: SAMURAI Study;
- illicit tobacco trade: traffic and consumer study;
- bar-OH: The figure of the publicans and alcohol. Occupational risks, drinking practices and risk reduction strategies in bars;
- STEPS – Exposure to tobacco during pregnancy: consistency of DNA methylation markers between tissues, persistence through childhood and the role of parents' socioeconomic status;
- development of a strategy to fight foetal alcohol spectrum disorders: evaluation of the appropriateness of pre-conception consultations;
- TORECAMMI – Mortality from tobacco-related cancers among migrants in France;
- predictors of success and benefits of abstinence from alcohol during "Dry January".

Junior researcher collaborative seminar 2022

The call for applications from "junior researchers in tobacco and/or alcohol" is organised in two selection phases. After the first stage of pre-selection based on letter of intent, a collaborative seminar is organised with and for the pre-selected applicants to prepare their full proposal and interviews. They have the opportunity to challenge themselves and to benefit from the feedback and advice of scientific experts. In addition, this meeting contributes to the development of a multidisciplinary community of researchers in the field of tobacco and alcohol.

The seminar was held on 6 May 2022 at the Institute's premises, and thirteen junior researchers presented and discussed their proposals at the event. Two experienced researchers and a laureate of the 2021 edition of this call also participated in the event to share their experience in designing, coordinating and managing research proposals with the applicants.

TABLE 29
FEATURES OF THE PROGRAMME FOR JUNIOR RESEARCHERS IN TOBACCO AND/OR ALCOHOL IN 2022

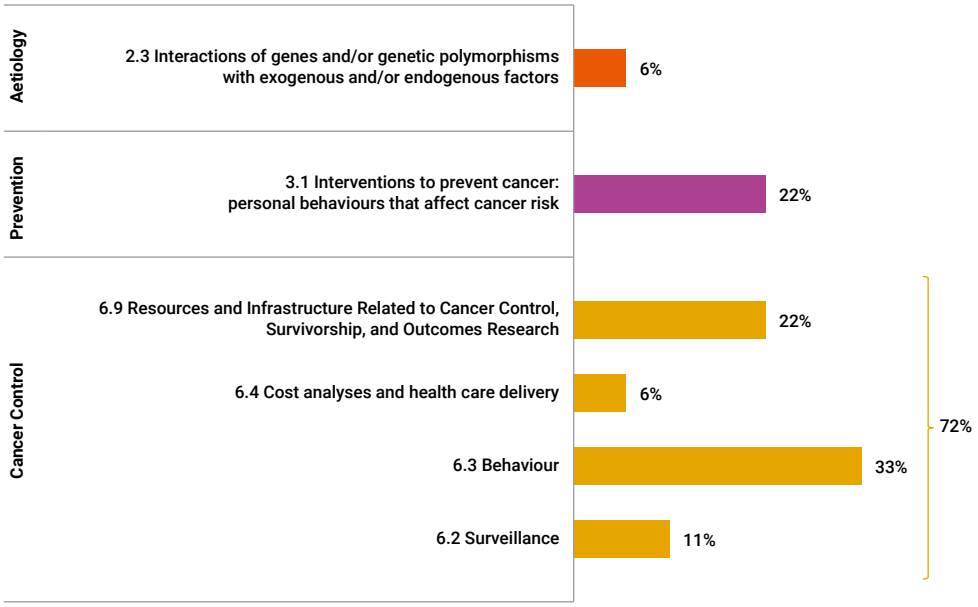
Programming institution	INCa
Operating institution	INCa
Funding institution	INCa
Funding	€976,279
Proposals submitted	18
Projects selected	9
Selection rate	50%

The projects selected thus cover a variety of themes, such as exposure to tobacco and alcohol, addiction care, and the evaluation of intervention programmes.

Among the selected projects, the distribution according to the substance studied remained balanced (5 relate to tobacco and 4 to alcohol). In terms of distribution by discipline, more than half of the projects are in the field of public health (5 projects). The other 4 projects are spread across several disciplines from human and social sciences (2 in sociology, 1 in psychology, and 1 in history).

We also notice a strong interest from junior researchers selected in studying populations who are considered vulnerable. Of the 9 applications selected, 3 focus on tobacco and alcohol consumption and exposure among pregnant women and young children, 2 on migrant populations, and 1 on the illicit tobacco trade in disadvantaged neighbourhoods.

FIGURE 28
DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE PROGRAMME FOR JUNIOR RESEARCHERS IN TOBACCO AND/OR ALCOHOL IN 2022



Support for research on environmental risk factors

CHLORDECONE CONSORTIUM

Chlordecone is an organochlorine insecticide that was used in the French Antilles (Guadeloupe and Martinique) between 1972 and 1993 to control the banana root borer. This highly stable persistent organic substance detected in soils is likely to contaminate some food products of plant or animal origin, as well as aquatic environments. In addition, surveillance data show that the incidence rate of prostate cancer is higher in the French Antilles compared to metropolitan France.

Therefore, the question arose as to whether exposure to chlordecone, both in banana plantation workers and in the general population through food, water and air, could lead to an increased risk of prostate cancer onset.

The National Scientific steering committee for research on chlordecone: CPSN chlordecone

Contribution to the chlordecone IV plan (2021-2027)

The National chlordecone IV plan was launched in 2021. The research programme on chlordecone and prostate cancer led by the multidisciplinary consortium is part of this plan, and corresponds to the 12th measure of the research area. The Institute is involved in the national governance body for the research actions included in the chlordecone IV plan. It is the national scientific steering committee for chlordecone, composed of scientific experts, ministries, and public health agencies. INCa contributed to the international conference on chlordecone held in Guadeloupe on 12 to 14 December 2022. Moreover, INCa was involved in drafting the knowledge summary document on chlordecone for the population.

In this context, and following a request from the Ministry of Health, INCa has set up a call for applications for an integrated and multidisciplinary cross-cutting research programme to better understand the link between chlordecone exposure and prostate cancer. This call for applications was built in collaboration with a scientific committee composed of national and international experts and with a support committee composed of French public organisations, as well as national and local agencies and stakeholders concerned by the issue.

Four applications were selected, and an additional expert was included later on in order to complete the consortium's areas of expertise. The expertise of the consortium covers the fields of epidemiology, biology and toxicology, human and social sciences, and knowledge of the French Antilles

The research programme was finalised in October 2021. With a budget of €3.45 million, it covers four areas of work: 1/ study of pre-existing data (2010-2019) from the general cancer registries and from exposure assessment mapping; 2/ set-up of a new epidemiological case-control study in Martinique; 3/ study, in Martinique and Guadeloupe, of the individual experience, social mobilisations and institutional structures related to pesticide contamination, including chlordecone; 4/ evaluation of the distribution of chlordecone in blood, adipose tissue and prostate tissue, as well as the effects of chlordecone exposure on markers of prostate cancer aggressiveness.

The governance of the consortium was formalised in June 2022 with the development of an operation and ethics charter.

The first annual meeting of the support committee took place in November 2022.

SUPPORT FOR THE NATIONAL ENVIRONMENTAL AND OCCUPATIONAL HEALTH RESEARCH PROGRAMME (PNR-EST) OF THE FRENCH NATIONAL AGENCY FOR FOOD, ENVIRONMENTAL AND OCCUPATIONAL HEALTH AND SAFETY (ANSES) BY ITMO CANCER-AVIESAN

This multi-agency programme addresses various public health issues related to the environment and workplace. ITMO Cancer-Aviesan has been funding cancer-related projects within this programme since 2011.

TABLE 30
FEATURES OF THE PNR-EST PROGRAMME IN THE CANCER FIELD IN 2022

Objectives	• To evaluate the risk of cancer linked with exposure to potential carcinogens in the general population or at work. • To analyse the effects of low-dose or cumulative exposures of CMRs on cancer risks. • To identify environmental or occupational cancer risk factors. • To analyse gene/environment/behaviour interactions on cancer risks. • To develop cost/benefit assessment methods for cancer prevention or care. • To identify and validate biomarkers allowing cancer risk estimation in occupational or environmental settings.
Programming institution	Anses
Operating institution	Anses
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€555,000**
Projects funded	3

The projects funded in 2022 were aimed at estimating the risk of ionising radiation (IR)-induced central nervous system (CNS) cancer death with respect to the occupational IR dose received (case-control study); understanding the link between external and internal exposome in lung carcinogenesis in non-smoking women; evaluating the impact of road traffic-induced atmospheric pollution on the risk of cancer in childhood.

SUPPORT FOR THE NATIONAL ÉCOPHYTO 2+ PROGRAMME FROM THE FRENCH OFFICE FOR BIODIVERSITY BY ITMO CANCER-AVIESAN

The French national Écophyto 2+ plan aims to reduce phytopharmaceutical compound use, dependence, risks and impacts by supporting changes in practices. In this context, the French Office for Biodiversity and the Ministries overseeing the Écophyto 2+ plan launched a call for proposals aimed at exploring the human health and ecosystem effects of exposure to these compounds. ITMO Cancer-Aviesan supports this initiative by funding some projects (3 since 2020).

2022:
1
project funded
for a total amount of
€500,000

TABLE 31
FEATURES OF THE ÉCOPHYTO 2+ PROGRAMME IN THE CANCER FIELD IN 2022

Objectives	To support projects exploring the effects of phytopharmaceutical compound exposure on cancer.
Programming institution	French Office for Biodiversity
Operating institution	French Office for Biodiversity
Funding institution	Inserm for ITMO Cancer-Aviesan
Funding	**€500,000 (1 project)**

In 2022, the project funded was aimed at characterising the impact of pesticide exposome on lymphomagenesis, chemoresistance and survival outcomes.

Support for professional careers and training

RESEARCH CHAIR IN HUMAN AND SOCIAL SCIENCES AND PUBLIC HEALTH ON TOBACCO AND CANCER PREVENTION

After a number of positive experiences in creating chairs to promote research in human and social sciences and intervention research applied to cancer, in 2022, INCa launched a research chair on "Tobacco and cancer prevention".

In line with the ten-year strategy and the guidelines of the Addictions Fund (managed by CNAM), the purpose of this chair is to bolster and revitalise research into the prevention of tobacco-related cancers, with a particular focus on cross-disciplinary issues (combatting social inequalities, accounting for vulnerable and specific populations) and on methodological approaches that contribute to reflection around intervention methods and participatory approaches.

The chair was awarded to Maria Melchior, an epidemiologist at Inserm, affiliated with Institut Pierre Louis d'Epidémiologie et Santé Publique (IPLESP) and with Equipe de Recherche en Epidémiologie Sociale (ERES). Her research focuses on social inequalities in mental health, with a particular emphasis on developmental trajectories from childhood to adulthood and intergenerational transmission of psychiatric disorders.

The budget allocated to the chair is €750,000 for five years (funding by the Addictions Fund, which is managed by CNAM).

PHD PROGRAMME IN HSS-E-PH

For the 12th consecutive year, the French National Cancer Institute launched in 2022 a call for applications to provide four doctoral grants in order to promote research in human and social sciences, epidemiology and public health (HSS-E-PH) applied to cancer control. A total of 27 applications were submitted to INCa and one of these was classified as out of scope. The 26 reviewed proposals are split into three research categories. Table 32 presents the distribution of the applications reviewed. The distribution of projects according to discipline is on the whole consistent between 2021 and 2022.

TABLE 32
DISTRIBUTION OF REVIEWED PROPOSALS UNDER THE PHD PROGRAMME IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH

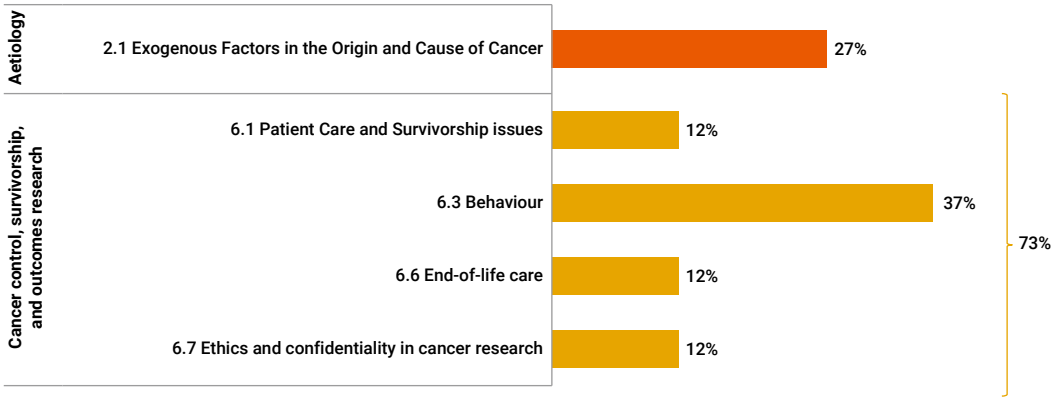
Research categories	Number of applications
Social sciences (sociology, anthropology, geography, management sciences, economics, political science, social marketing, etc.)	9
Epidemiology or biostatistics	8
Human sciences (psychology, cognition and learning, psychoanalytic studies, exercise science, etc.)	9

Following the review process, including interviews of applicants, four PhD theses were selected for funding (Table 33).

TABLE 33
DOCTORAL FELLOWSHIPS FUNDED IN 2022

Title	Discipline
Exposures to pesticides near agricultural plots and risk of acute childhood leukaemia	Epidemiology
Health promotion through physical activities: professional practices of nurses and social reception of patients	Sociology
Preserving patient autonomy: the role of physicians in adopting anticipatory directives in oncology	Ethics
Dispositional optimism in children and adolescents with cancer and their families: what role(s) in psychosocial adjustment to the disease and its potential traumatic impact?	Psychology

FIGURE 29
DISTRIBUTION OF THE SELECTED GRANTS ACCORDING TO THE CSO CLASSIFICATION IN 2022



In 2022, 4 PhD students were awarded funding in the following disciplines: ethics, epidemiology, sociology, and psychology.

PhD meeting

Since 2020, the Institute has set up a specific support and animation system for doctoral students funded by the Institute via the HSS-E-PH and SPADOC calls for applications. These include annual meetings, which are intended to create a space for exchanges between doctoral students by allowing them to present their work; to meet other doctoral students, researchers and other stakeholders in the fight against cancer; and to encourage a multidisciplinary research dynamic. In addition, this organisation contributes to the Institute's influence and helps to build a multidisciplinary community of researchers in the field of cancer control. This process therefore meets the objective of breaking down disciplinary barriers as set out in the Ten-year cancer control strategy and in the Institute's action plan.

In 2022, for the third edition, 29 PhD students met for two days on 16 and 17 September on the Cély campus in the Seine-et-Marne region.

The programme of these meetings was co-constructed with the doctoral students, in order to best meet their expectations and needs. The theme of these meetings was the communication of research to the general public. After a visit to the temporary exhibition on cancer at the Cité des Sciences et de l'Industrie in Paris, an institutional introduction and a presentation of the funding schemes, the sessions were organised by themes (aetiology, prevention, screening, etc.) around presentations of the PhD students' thesis work, followed by some time for discussion.

REVIEW OF CANCER RESEARCH FUNDING

Cancer research funding in 2022

In 2022, 328 projects were selected and the total funding awarded to cancer research programmes amounted to over €214.3 M, including:

- €131.6 M from INCa;
- € 51.4 M from DGOS;
- €31.3 M from Inserm for ITMO Cancer-Aviesan.

Figure 30 shows the breakdown of multi-year funding for 2022 according to programme type:

- investigator-driven projects concerning the 4 major research areas (biology, translational, clinical, human and social sciences, epidemiology, and public health);
- strategic research initiatives and thematic programmes encompassing INCa's actions to support precision medicine, the intervention research programme operated and funded by INCa, the integrated programme addressing tobacco control in partnership with IReSP, and thematic research programmes managed by ITMO Cancer-Aviesan;
- support for platforms, resources, and infrastructures;
- research training and support for young teams of excellence, especially covering the PhD programme in human and social sciences, support for chairs, ATIP-Avenir, and translational research training programmes for medical doctors, pharmacists, and veterinarians.

This figure shows that 34% of the allocated budget was devoted to competitive investigator-driven projects, with calls managed by INCa. This year was marked by a significant increase in the budget mainly due to the canceropole and SIRIC designation rounds (for 5 years), the clinical and translational research programmes whose launch had been delayed, and the new calls included in the Ten-year strategy.

FIGURE 30
2022 MULTI-YEAR CANCER RESEARCH FUNDING BY PROGRAMME TYPE (INCA, DGOS, ITMO CANCER-AVIESAN)

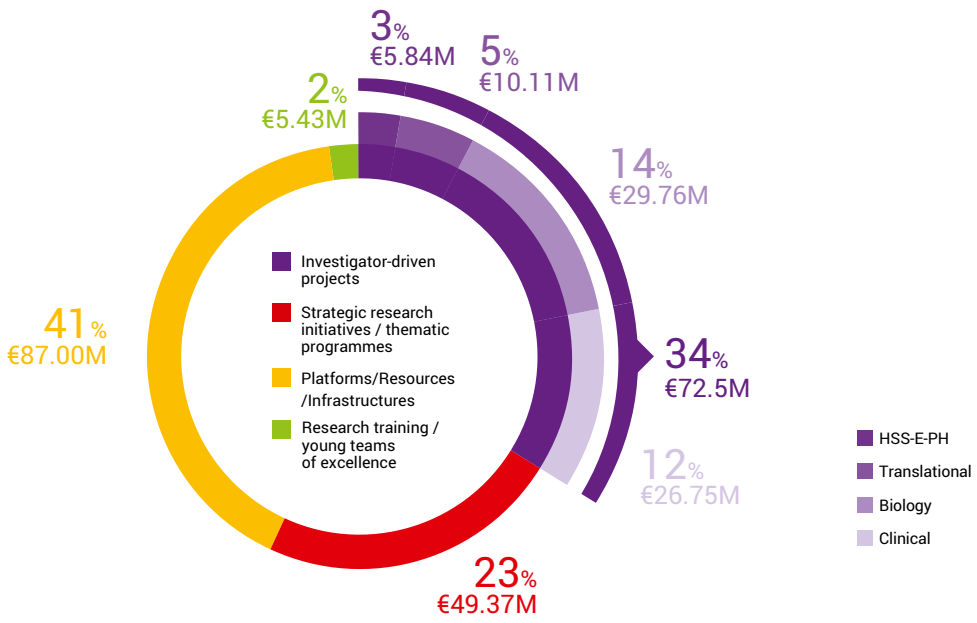
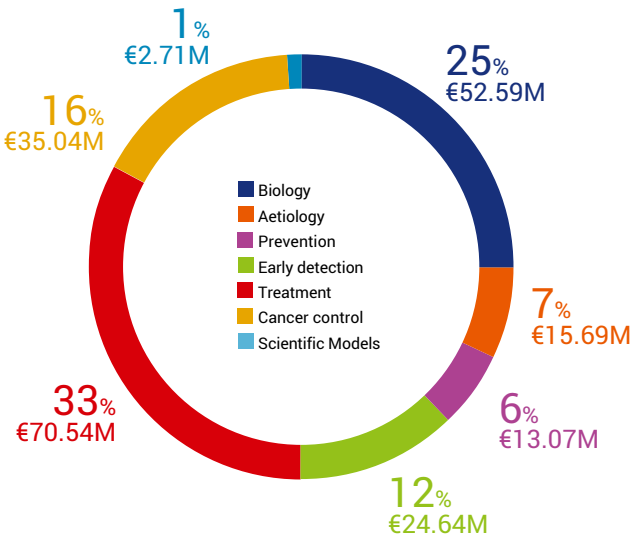


Figure 31 presents the 2022 funding allocation according to the CSO classification:

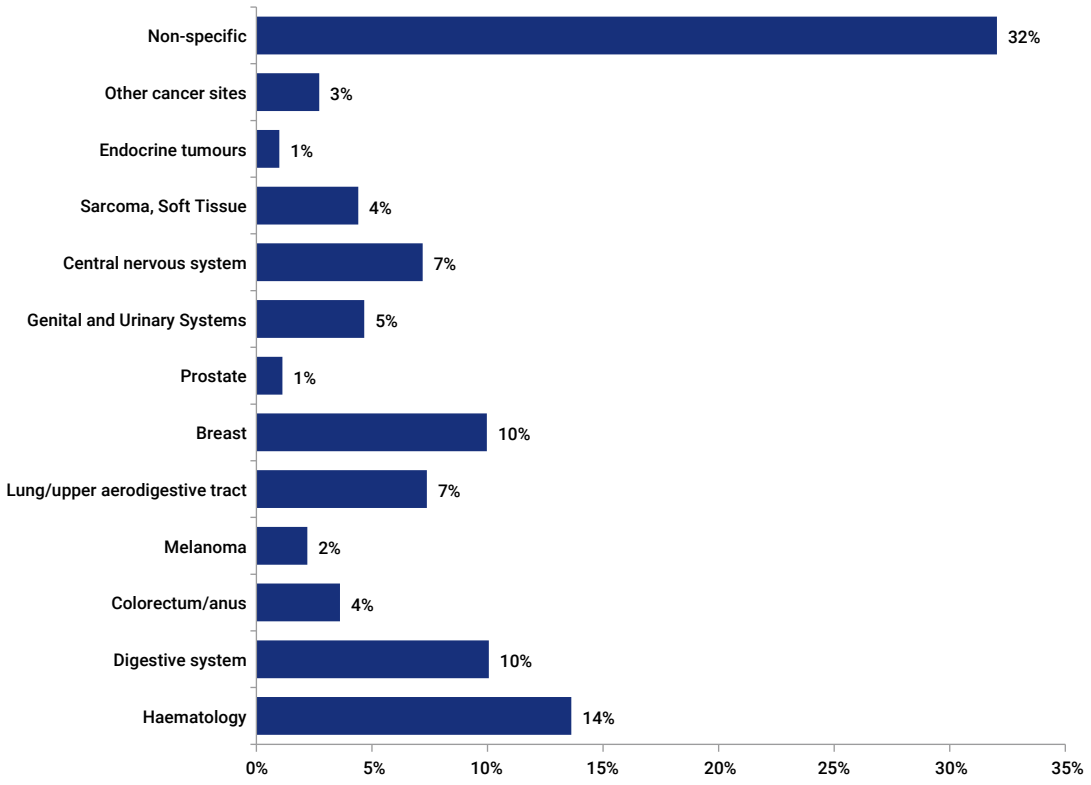
- the biology category represented a significant investment with €52.6M (25%);
- treatment and early detection, diagnosis and prognosis amounted to €70.5M and €24.6M respectively (33% and 12% of investments);
- studies relating to the aetiology category amounted to €15.7M and represented 7%;
- cancer control, survivorship, and outcomes research issues represented 16% of investments (€35M), while the prevention category represented 6% of investments (€13M).

FIGURE 31
2022 MULTI-YEAR CANCER RESEARCH FUNDING ACCORDING TO THE CSO CLASSIFICATION



The breakdown of 2022 funding by cancer sites studied shows that 32% of the allocated budget was non-specific to a tumour type, representing over €68.7 M (Figure 32).The main cancer sites studied were haematology, digestive system, and breast.

FIGURE 32
2022 MULTI-YEAR CANCER RESEARCH FUNDING BY CANCER SITES STUDIED



Cancer research funding over the 2007-2022 period

Since 2007, a total of 4,118 projects have been funded through the different competitive calls for research proposals and grants for designation representing over €1.67 Bn.

Figure 33 shows the breakdown of total funding for 2007-2022 by programme type:

- investigator-driven projects of the four main research areas represented a total of 48% of 2007-2022 investments, or approximately €790.8M;
- strategic research initiatives aimed at primarily supporting precision medicine initiatives and thematic programmes represented 26% of cancer research investments (€438.5M);
- support for resources and infrastructures represented nearly 23% of total funding, approximately €386.1M, which highlights the drive to reinforce the organisational framework and the coordination of cancer research activities. Alongside support for investigator-driven projects, INCa has developed a proactive policy for fostering cancer research excellence through the designation of and support for dedicated infrastructures aimed at promoting coordinated, integrative, and effective cancer research;
- support for young teams and cancer research training represented a total of 3% of total investments (€58.7M).

FIGURE 33
2007-2022 MULTI-YEAR CANCER RESEARCH FUNDING BY PROGRAMME TYPE

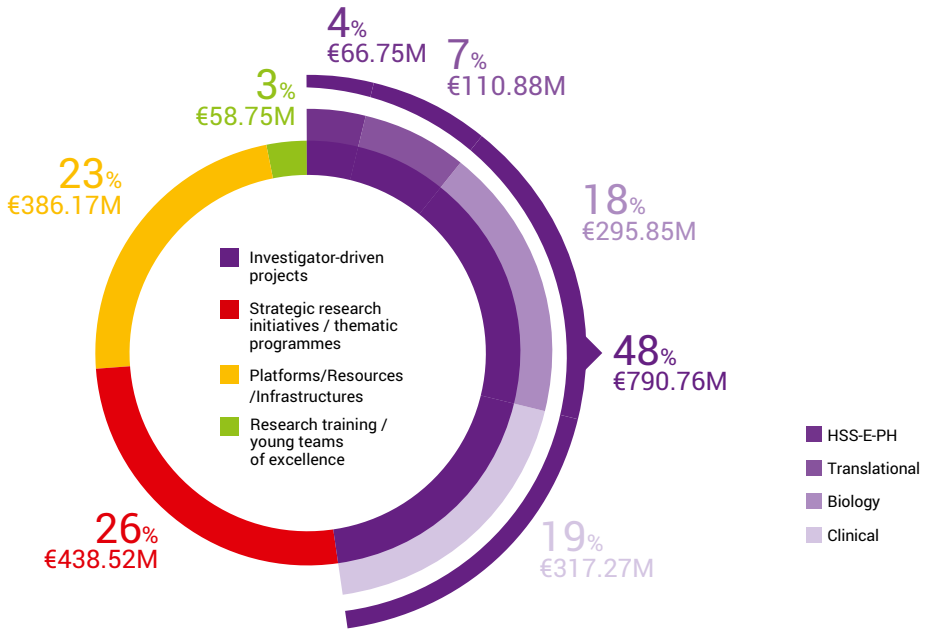
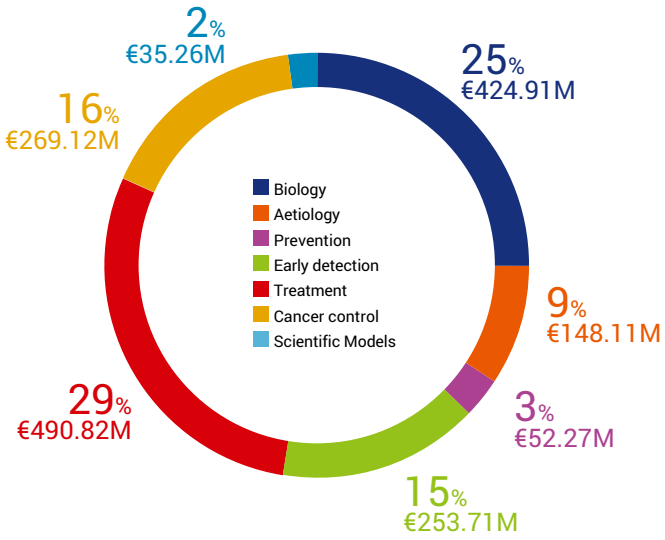


Figure 34 presents the distribution of total funding for 2007-2022 according to the CSO classification:

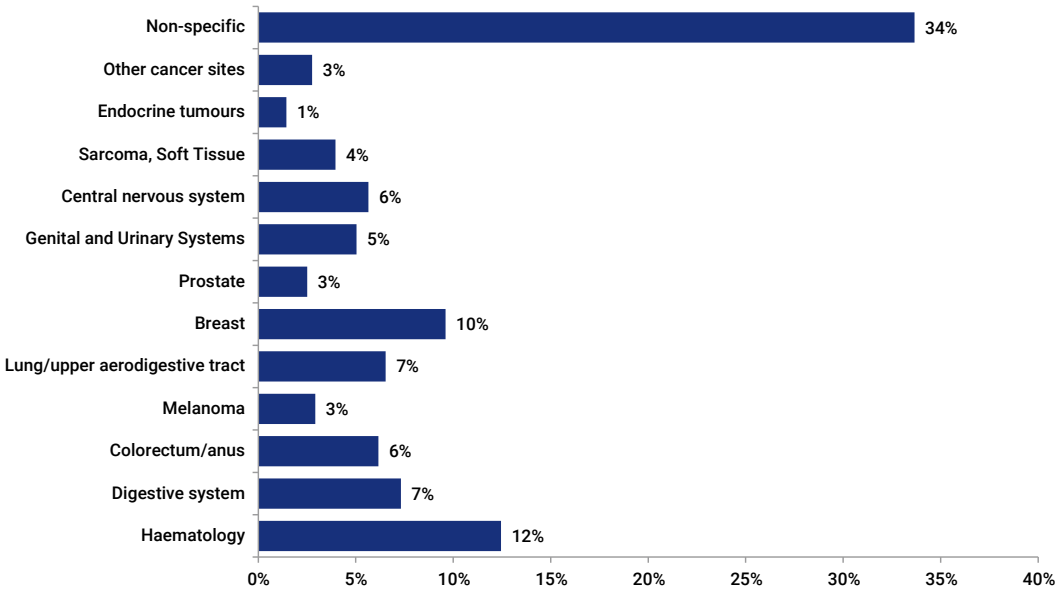
- the treatment and biology categories represented the most significant investment, with €490.8M and €424.9M, respectively;
- cancer control, survivorship, and outcomes research issues represented 16% of total funding (€269.1M);
- the early detection, diagnosis and prognosis categories amounted to €253.7M;
- research aimed at identifying the causes or origins of cancer – genetic, environmental, and lifestyle – and the interactions between these factors falls under the aetiology category, representing 9% of total funding with €148.1M;
- the prevention and scientific model categories amounted to €52.3M (3.1%) and €35.3M (2.1%), respectively.

FIGURE 34
2007-2022 MULTI-YEAR CANCER FUNDING ACCORDING TO THE CSO CLASSIFICATION



Over the 2007-2021 period, 34% of the budget was allocated to non-specific cancer types (Figure 35). Haematological malignancies and breast cancer represented 12% and 10% of investments, respectively.

FIGURE 35
2007-2022 MULTI-YEAR CANCER FUNDING BY CANCER SITES STUDIED

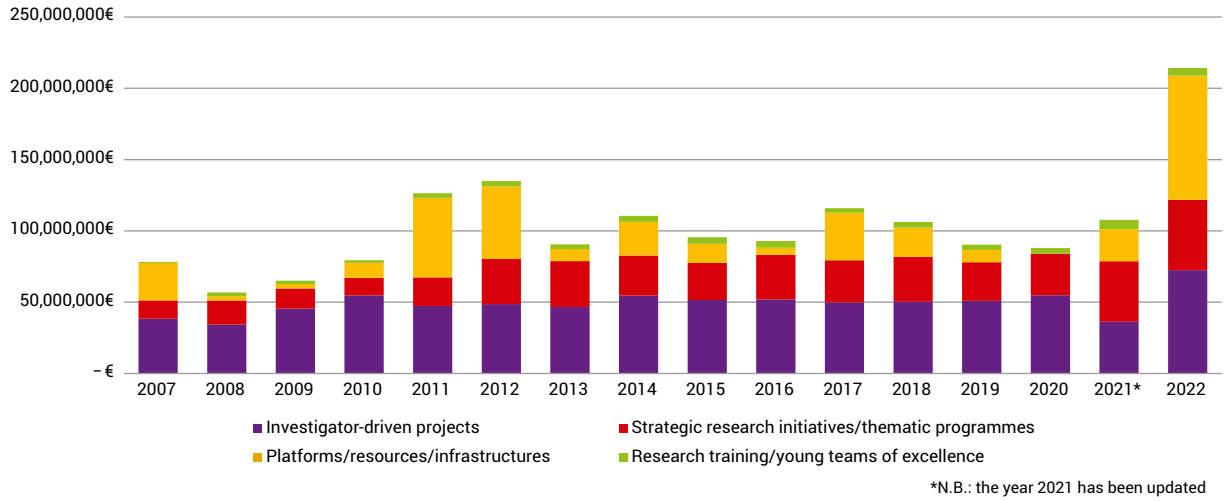


Trends in cancer research investments

Figures 36 and 37 present the trends in total funding according to the programme type and cancer research fields over the 2007-2022 period, respectively.

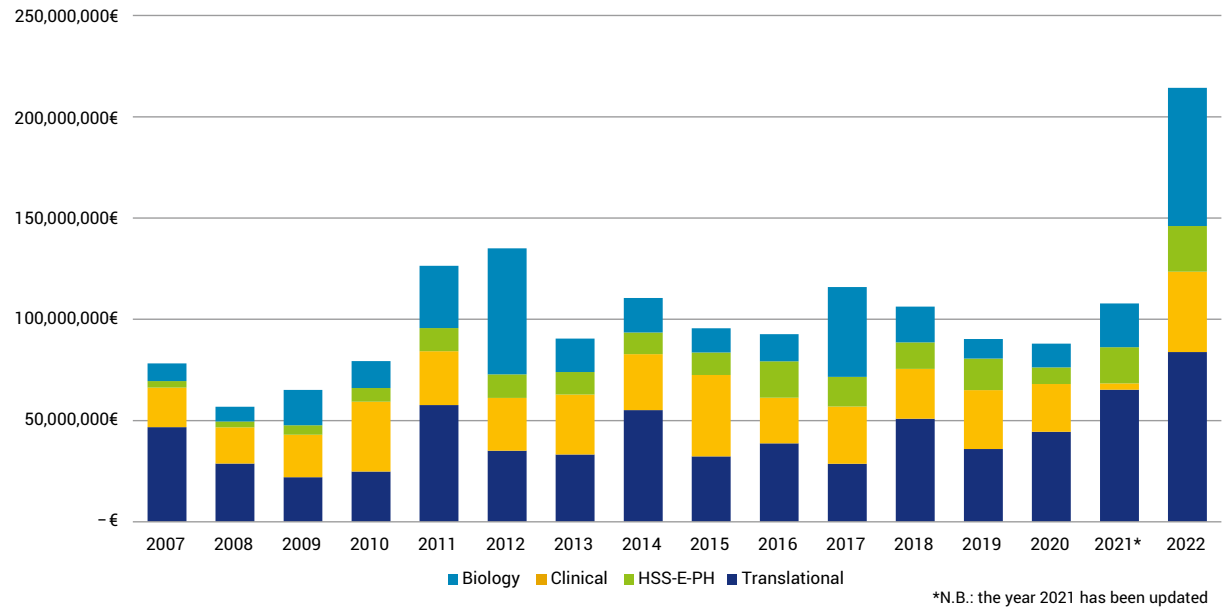
The different structures supported in recent years have delivered significant multidisciplinary synergistic interactions for research funding and drug access to patients, and have provided a basis for the coordination of clinical, fundamental, and human and social science research at a regional level in France. Coordinating, maintaining, and reinforcing them to provide integrated and coordinated cancer research on a nationwide level is a key objective for the French National Cancer Institute.

FIGURE 36
TRENDS IN TOTAL FUNDING ACCORDING TO PROGRAMME TYPE OVER THE 2007-2022 PERIOD



*N.B.: the year 2021 has been updated

FIGURE 37
TRENDS IN TOTAL FUNDING ACCORDING TO CANCER RESEARCH FIELD OVER THE 2007-2022 PERIOD



*N.B.: the year 2021 has been updated

Ten-year cancer control strategy-review of cancer research funding

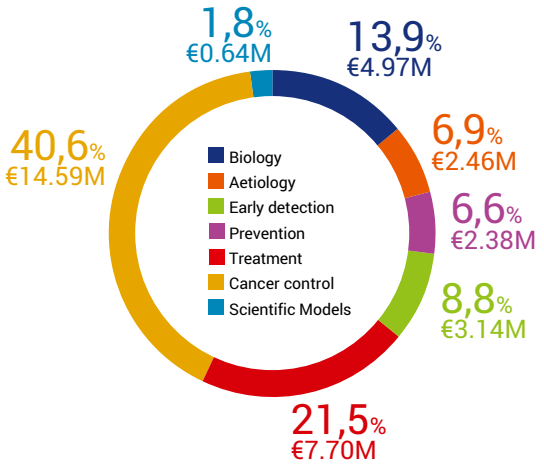
The year 2022 was marked by the launch of numerous calls for projects dedicated to the Ten-year cancer control strategy, which is structured around 4 strategic challenges:

- improving prevention;
- reducing sequelae and improving patients' quality of life;
- addressing cancers with poor prognosis;
- ensuring that everyone benefits from progress.

The Strategy is organised around 234 measures and the Institute has proposed a 2021-2025 roadmap. In 2022, 120 actions were already launched, including cancer research actions.

Nine calls for research proposals were launched (objectives described above). In total, in 2021-2022, €35.8 M (72 projects) has been earmarked for the Ten-Year Cancer Control Strategy (Figure 38). The breakdown of 2021-2022 funding by studied cancer sites shows that 41% of the budget was non-specific to a tumour type, representing over €14.5 M. The main studied cancer sites were the digestive system, lung/upper aerodigestive tract, and haematology.

FIGURE 38
DISTRIBUTION OF SUMS ALLOCATED FOR THE TEN-YEAR CANCER CONTROL STRATEGY RESEARCH PROGRAMMES ACCORDING TO THE CSO CLASSIFICATION



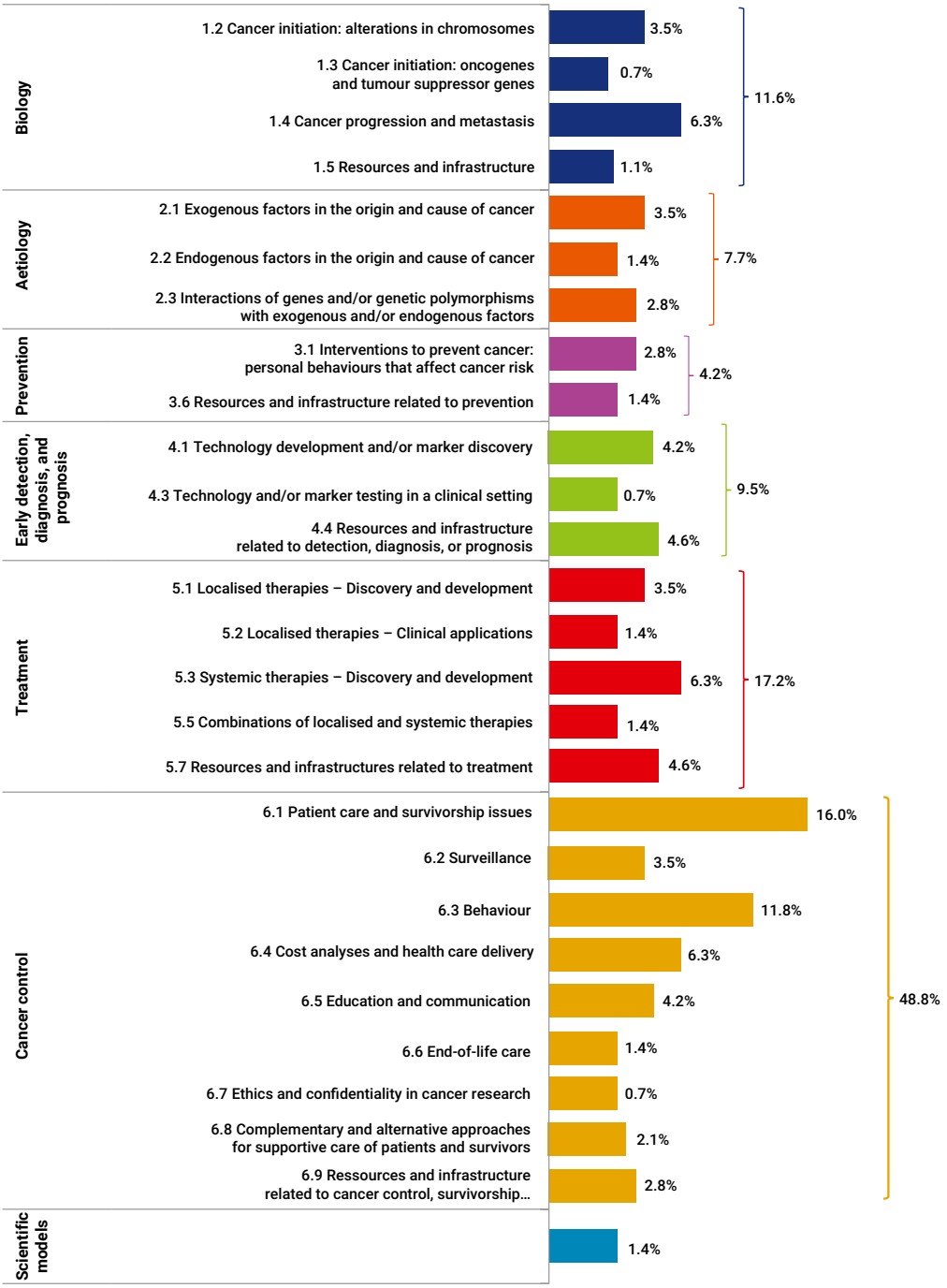
ITMO Cancer-Aviesan 2011-2021 activity report

The role of ITMO Cancer-Aviesan in the design and implementation of successive cancer control plans during the 2011-2021 period was the subject of an assessment published in July 2022. The brochure "ITMO Cancer-Aviesan 2011-2021: A decade of involvement in the Cancer Plans" presents an overview of:

- its contribution to the definition of the research strategy within the framework of the 2nd and 3rd Cancer Plans and the 2021-2030 Ten-Year Strategy;
- its leading role in the programming of thematic and multidisciplinary basic research on cancer;
- its historical mission of supporting the French cancer research community.

FIGURE 39

DETAILED ANALYSIS OF THE DISTRIBUTION OF FUNDED PROJECTS FOR THE TEN-YEAR CANCER CONTROL STRATEGY OVER THE 2021-2022 PERIOD ACCORDING TO THE CSO CLASSIFICATION



RESEARCH IMPACT AND SOCIETY

Open science

FRENCH NATIONAL RESEARCH FUNDING AGENCIES – TOWARDS THE IMPLEMENTATION OF AN OPEN SCIENCE POLICY – 2022 HIGHLIGHTS

On 29 June 2020, five national research agencies (French Agency for Ecological Transition-ADEME; French National Research Agency-ANR; French National Food, Environment and Occupational Health Safety Agency- ANSES; French National Cancer Institute-INCa; French National AIDS and Viral Hepatitis Research Agency-ANRS MIE) signed a Joint Declaration to support open science. Since then, all the agencies have adopted strong commitments and implemented a common policy. In 2022, a joint report was published; the main conclusions are as follows

- ***Promoting open access for funded project publications***

All the agencies have applied the same open access policy, requesting the sharing of scientific publications in the national archive (HAL) or via a local institutional archive. In addition, they have recommended publishing in open-access journals. In accordance with the second National Plan for Open Science, all the national research agencies are committed to implementing the rights retention strategy.

- ***Promoting data openness***

In order to prepare the sharing and/or dissemination of the dataset in compliance with the principle "as open as possible, as closed as necessary", each funding agency has requested a data management plan (DMP). The national research agencies have adopted the common model developed by Science Europe, which has been made available to researchers via the DMP OPIDoR website (national online DMP creation support tool)

Open Science – new commitment

For many years, the Institute has been involved, at a national and international level, in reforming the current evaluation system. As soon as this reform was set up in September 2021, INCa joined the French working group DORA. The purpose of this group was to bring together the French institutions that had signed the San Francisco declaration on research, and who wanted to implement open science concretely in their entire evaluation process. The conclusions of this working group were fed into the French contribution to the Open Science European Conference, held at the beginning of February 2022 (under the auspices of the French Presidency of the European Union). This conference provided an opportunity for many organisations (including INCa) to sign the Paris Call announcing the creation of a coalition of European research actors committing themselves to implementing operational transformations in their evaluation practices. This so-called Coalition for Advancing Research Assessment (CoARA) was set up and was joined by 351 organisations from over 40 countries, including INCa at the end of 2022. This coalition will come into effect in 2023.

- ***Sharing and harmonising our evaluation practices***

In accordance with the San Francisco Declaration and the Paris Call (see open science – new commitment section), all the agencies have

- continued to communicate to improve our practices when evaluating the scientific quality of projects;
- ensured that all research products are considered. This reflection is also in line with the implementation of the unique portal for submission (see below).

- ***Open science practices***

In 2022, a series of awareness-raising webinars were designed, especially for staff members, on the challenges of open science and its methods.

- ***Open funder dataset***

In agreement with the Open Government Partnership and in accordance with the Digital Republic Law, the national agencies have published all information relating to funded projects on data.gouv.fr (national open platform for French public data).

Evaluation

INTELCOMP PROJECT (2021-2023) – HCERES AND INCA PARTNERSHIP

Intelcomp is a Horizon 2020 innovation with the aim of building a cloud platform that will offer artificial intelligence-based services for science, technology and innovation (STI) policy. The project led by the "Fundación Española para la Ciencia y la Tecnología" (FECYT) brings together a European multidisciplinary team. The platform will be tested on 3 specific pilot cases of STI policy: artificial intelligence, climate change, and health. The Health Cloud Platform (HCP), launched in 2022, commissioned by the French High Council for Evaluation of Research and Higher Education, HCERES, specifically addresses cancer. Different actors have carried out numerous studies to describe and characterise cancer research by analysing scientific production through publications, patents, and clinical trials. The challenge of the Cancer Cloud Platform is, firstly, to be able to link funding with scientific production and, secondly, to characterise the medical and societal impact of cancer research. IntelComp could provide answers to these challenges thanks to the broad spectrum of integrated data in terms of funded projects and in terms of impact on medical practices as well as on economic and social issues. The mobilisation of IntelComp's AI technology will make it possible to analyse the congruence between scientific research priorities and policies, societal burden, or demands and impact on public health.

Participatory research

The Institute is committed to encouraging participatory research, also known as citizen science or *community-based research*. According to the charter of participatory science and research in France (Charte des sciences participatives en France, 2017), this research consists of "forms of scientific knowledge production in which civil society participates, individually or collectively, in an active and deliberate way". It is research "by" or "with" citizens rather than "on" or "about" them.

This initiative is part of the Ten-Year National Cancer Control Strategy (2021-2030), and is in line with our commitments to supporting open science.

The first step of this project has entailed benchmarking cancer research initiatives, both nationally and internationally. We started this benchmarking process (scientific literature review and interviews) during the second semester of 2022. The literature review carried out so far has provided different ways to involve patients and civil society in research dynamics, such as: advisory bodies, working groups, dedicated call for proposals, networking platforms, or actual involvement in research projects. This research has also highlighted the importance of involving patient organisations, as they can contribute with their data, which can be used for research purposes, offer their own specific expertise, set research priorities or topics for calls for proposals, and take an active part in the evaluation process. The goal is to involve them in cancer research and other stakeholders such as peer caregivers, patients' families, and society as a whole. A roadmap will be defined in the coming year, taking this analysis into account.

Funding agency data appear to be a particularly relevant application for Intel-Comp. The area of greatest interest for INCa is the analysis of the impact of funded research projects and the characterisation of "impact pathways". The funder can ask questions upstream of funding (which field to be funded, which team etc.) and downstream (what are the scientific findings of funded projects, what are the societal goals, etc.). In the future, all funders can share a common type of use case.

The goal of this use case is to be able to trace and monitor a wealth of indicators in four major pillars measuring:

- *Outputs*: publications produced by programme/funder, publications cited in patents, patents produced;
- *Medical impact*: publications cited in medical guidelines, innovations in terms of diagnostic tools, treatments, drugs, new therapies;
- *Economic impact* by tracking innovation performance of companies (enterprises with evidence of innovation activities and medical technologies);
- *Societal impact* indicators in three dimensions: societal awareness/relevance of research, congruence of research funding with societal priorities, and impact on public health.

The first HCP activity has essentially been devoted to:

- identifying the spectrum of data needed and tools making it possible to connect these data together and to link them to funded projects;
- trailing tools from Intelcomp to connect data together and visualise results.

In 2023, the objectives of the HCP are to make stakeholders converge and deliver technical possibilities.

Analysis of publications and patents related to cancer worldwide (2003-2019) – launch of study

The evaluation of scientific research is a major issue and bibliometrics is one of the methods for establishing benchmarks of scientific productivity. It is also a public policy support tool that allows international comparisons.
In 2017, INCa published specific data on French cancer research (publications and patents) for the 2003-2015 period. This study showed that despite increased competition in recent years, France was still one of the most competitive countries in the field of cancer research.
The implementation of Cancer Plans has undoubtedly contributed to this dynamic. Indeed, the international visibility of French cancer research seemed to have increased since the launch of the first French Cancer Control Plan.

The objectives of this study are to:

- update data (publications and patents) for the 2003-2019 period;
- establish the French positioning on some specific research fields;
- obtain a first analysis of French publications focused on cancers with poor prognosis (strategic area of the Ten-year strategy). A new analysis will be performed in 2023.

French research funders working group – National Roadmap implementation

In the appended report of the research programming law (Loi Programmation Recherche, 2021), a unique submission portal intended for all calls for research proposals launched by national funding agencies has been included with the aim of facilitating and simplifying submission process for researchers.
The first step consisting in simplifying access to researchers and gathering information from calls from 6 funding agencies (ANR, ANSES, INCA, INSERM, ANRS, ADEME) has been in place since the beginning of the year. The next step will be devoted to harmonising application information and formats between funding agencies. Persistent identifiers (for example, ORCID) will be implemented to bring the researcher's full information (identity, career, research productions, etc.) together easily. The members of the working group are delighted that the recommendations issued in 2018 are fully included in this IT development. This project coordinated by the ANR (French National Research Agency and member of the French research funders working group) is funded by the Ministry of Research and Innovation.

Strategic foresight analysis

Cancer research lends itself particularly well to prospective exercises as it deals with long-term issues. This discipline contributes to the identification and better anticipation of trends, disruptions, and emerging topics likely to represent key issues for research in the years to come. Within the scope of the Ten-Year National Cancer Control Strategy (2021-2030), the Institute is committed to developing a foresight analysis to identify the main drivers of change, disruptions, weak signals or emerging topics which could influence cancer research and impact the health of the general population and people with cancer, in the next 15 to 20 years. This analysis should therefore help us respond to the strategic challenge of anticipating and identifying future research issues, with the goal of informing future decisions and contributing to the definition of the future cancer control strategy in collaboration with all stakeholders. As a starting point, national and international benchmarking was carried out during the second semester of 2022, to identify best practices among the health agencies which have implemented this type of approach.

The benchmarking helped identify methods of foresight analysis and their implementation in national and international institutions, particularly in public health and oncology research. Methods to identify key issues in future cancer research found in the benchmarking process were:

- international networking and communication events aimed at providing an overview of the state of the art in certain areas of cancer research, and at encouraging the emergence of new concepts for combined approaches to benefit patients;
- scenarios and quantitative simulations such as those
  - used by the European Commission cancer mission for their foresight analysis for the Horizon Europe mission board imagining health in Europe in 2050
  - or developed at a national level like the Ontario Institute for Cancer Research (OICR) to help develop their strategic plan for 2021-2026;
- or key recommendations developed by national or international agencies.

Based on this analysis, a tender will be published in 2023. The objective is to support us in the scoping phase and in carrying out this first prospective analysis. It is proposed that the International scientific advisory board will be commissioned for this exercise (role to be specified).

3

Strategic orientations for advancing cancer research

Cancer is a formidable adversary that must be tackled using all available tools. The French National Cancer Institute, INCa, is dedicated to this fight, in coordination with ITMO Cancer.

INCa's research efforts in 2022 increased significantly through new actions implemented in line with the national Ten-year strategy. They also provided ongoing support for recurrent calls for basic, translational, and clinical investigations, as well as specific actions in human and social sciences, cancer screening, and prevention. These recurrent calls now represent the core funding for research operators in France. Approximately fifty percent of funding is allocated to investigator-driven projects, a threshold that needs to be maintained to continue supporting free-minded research.

In addition to project support, INCa promotes and contributes to structuring cancer research sites. This policy was initiated ten years ago with the SIRIC programme, to build competitive comprehensive cancer centres. This strategy continued in 2022 with a new set of SIRIC centres and preparations for a new call to implement their paediatric version. Numerous other calls focusing on collaborative research networks have been issued. Step by step, the cancer research landscape is taking shape, with centres of excellence capable of producing breakthrough findings rather than incremental research.

In addition to this national effort, INCa is establishing new international partnerships. The questions raised by cancer research require a greater order of magnitude of resources and a diversity of expertise. Rising costs, data complexity, growing requirements for computer sciences, and the continuous flow of new technology necessitate collaborative networks that cannot operate efficiently solely at a national level. This trend, which has been observed in other scientific disciplines such as physics decades ago, needs to be considered in research agencies' strategies. INCa is partnering with Japan, the UK, and Europe to support international calls.

All of these actions could not have been implemented without the dedicated efforts of INCa's staff. I want to take this opportunity to thank them for their unlimited commitment to our fight against cancer.

Prof. Bruno Quesnel
Director of Research and Innovation Division – Institut National du Cancer
Director of ITMO Cancer-Aviesan – INSERM

SUPPORT FOR BIOLOGY, TRANSLATIONAL AND INTEGRATED CANCER RESEARCH

Strong support for fundamental and translational cancer research remains a priority for the Institute. Substantial budgets will be committed again in 2023 for the PLBIO and PRT-K calls for proposals, to ensure that the selection rate for projects is in line with that set out in the French research programming law.

Numerous studies and actions were carried out in 2022 which will enable new actions to be implemented in 2023.

Thus in 2023, the following will be launched:

- an Integrated Research Action Programme (PAIR), aimed at promoting cooperation between all scientific disciplines (basic research, clinical research, epidemiology, public health and human and social sciences) around a core project, that will focus on the link between obesity and cancer (action I.1.4 of the Ten-Year Cancer Control Strategy). This call for proposals will be launched in collaboration with the French Ligue contre le cancer;
- a call for applications for the designation of research networks devoted to research on poor prognosis cancer (action III.1.1);
- a new Joint Transnational Call for Proposals 2023 (JTC 2023) focusing on "Translational research on cancer epigenetics" in the context of the European TRANSCAN network (aiming to promote a transnational collaborative approach between scientific teams in demanding areas of translational research to produce significant results of higher quality and impact, and to share data and infrastructures).

The following will be implemented:
- the new Canceropole Objectives and Performance Contract (taking into account the results of the Canceropole evaluation carried out in 2022) (see section 1.3);
- the 8 newly designated SIRICs (see section 2.3.1);
- leadership of the OSIRIS project (see section 2.3.1) will be taken over by the Institute.

In response to action II.3.2, indications for molecular tests for cancer patients with a view to prescribing targeted therapies for non-small cell bronchial cancer and for cutaneous or mucosal melanoma will be published.

Since 2019, fundamental paediatric cancer research has been awarded an additional annual €5 million earmarked for this topic. This funding, aimed at stepping up oncopaediatric research, reinforces the efforts of the French government, which has made research in paediatric cancer care a priority. In line with the objectives defined for the use of this budget, new calls for proposals for paediatric cancer research will be launched with:
- a third edition of the Call for applications "Paediatric cancer research: doctoral, postdoctoral grants and international mobility grants" to fund research theses or postdoctoral grants for paediatric cancer research (in France and abroad) or to help students (Master 2 and PhD students), postdoctoral fellows and statutory staff (researchers, medical doctors, engineers, etc.) conducting research in France to complete international internships/fellowships, in order to acquire new expertise for the development of paediatric cancer research projects;
- a second edition of the Call for proposals "Paediatric oncology research: contribution from interdisciplinary approaches" to foster the emergence of ambitious interdisciplinary research projects.

This year, another additional specific allocation of €20 million has been earmarked to strengthen paediatric cancer research in France through an amendment to the 2022 finance law. The Ministry of Research has selected a number of initiatives for the use of these funds, which will be implemented in 2023:
- the designation of several integrated Research Centres of excellence in paediatric oncology, covering both fundamental and translational research;
- the creation of senior international chairs.

CLINICAL CANCER RESEARCH

Clinical cancer research support remains an essential area of the Ten-year cancer control strategy. In addition to strengthening recurrent core actions, the clinical research department continues to launch new specific actions with additional budgets.

In order to address the global action **Developing research to reduce sequelae and improve patients' quality of life**, a second call for proposals will be launched for thematic projects on **supportive care**, **surgical reconstruction**, **preservation of fertility and its restoration**, **quality of life**. In order to promote multidisciplinarity, projects must be carried out by 2 teams from 2 different disciplines from the fields of fundamental, clinical research or in human and social sciences-epidemiology-public health, with this programme enabling the emergence of research projects of excellence in topics that may be under-represented in our usual calls for proposals. The first edition was already a success, and we hope the second will be even better with the establishment of different expert working groups, in order to mobilise the research community, before the launch of the call.

As in 2022, we also expect to be able to foster new projects specifically addressing therapeutic de-escalation questions, through the PHRC-K call thanks to funds (an extra €5 million) secured from the French Ministry of Health, which was a recommendation made by INCa's SAB.

Regarding the area relating to "combating cancers with poor prognosis", several actions will be continued to serve the global action **Ensuring patient access to innovative therapies in the context of clinical trials**:

- **Offering all patients the opportunity to participate in trials, open to more centres, including overseas**

A new series of several co-investigating centres for projects funded through the PHRC-K call will be opened overseas thanks to a specific budget allowing access to clinical research closer to home for patients in French overseas departments (DOM). This action also makes it possible to create links between investigators in mainland France and those in overseas departments in order to facilitate future collaborations.

- **Improving the clarity of the clinical trial offering (thanks to an updated and accessible portal)**

Clarity of the clinical trial offering will be ensured thanks to a new development of the French cancer clinical trials registry RECF. Clinical research operators will obtain access to the database through specific personal accounts and will be able to update information concerning their trials in real time (see Part II, section 3.4.4).

Other actions will be continued or launched to serve the global action **Developing research to serve poor prognosis cancers**, again for the area relating to "combating cancers with poor prognosis".

- **Launching new clinical trials (new methodologies; new models; AcSé)**

A new AcSé programme, considering 4 cohorts with different molecular abnormalities, was built in 2022, and two of these cohorts should start at the end of 2023. Unicancer, as the sponsor, will open more than 21 centres in comprehensive cancer centres and university hospitals in France for each cohort.

- **Designating research networks specialised in cancers with poor prognosis**

A national CAR-T cell network will be launched.

Serving the action **Ensuring that vulnerable populations are included in the conduct of clinical trials**, a study funded in 2022 in order to identify the socio-economic barriers and tools for inclusion in early-phase clinical trials will commence (patient inclusions).

Regarding our recurrent core actions, we will launch a new Early-phase clinical trial centre (CLIP²) designation period.

Regarding the need to assess the impact of our research funding as mentioned by INCa's SAB, we are carrying out a quantitative analysis of all the results and publications of projects funded by PHRC-K over the 2005-2016 period. A first draft of the report is expected after the summer of 2023.

STRATEGIC OUTLOOK IN HUMAN AND SOCIAL SCIENCES, EPIDEMIOLOGY AND PUBLIC HEALTH

The 2023 work programme is in line with the Ten-year strategy launched in 2021, and with previous activities. It will focus on a number of areas: providing financial support for research; promoting and disseminating knowledge; creating and coordinating researcher networks; assessing funding mechanisms and producing human and social sciences and public health data on cancer.

In terms of research funding, the Human and Social Sciences, Epidemiology and Public Health Department (SHS-E-SP) will continue to support future generations of researchers (students, PhD students) in this area, with the renewal of the calls for PhD grant applications in the fields of Human and Social Sciences, Epidemiology and Public Health, as well as Psychoactive Substances and Addictions. The research scheme for young researchers in the field of smoking and alcohol piloted in 2020 was a great success in its first year and will be run again this year.

It will be launched along with the combined call for projects in the field of human and social sciences and intervention research (PHIR), with both open areas and themed areas. This call for proposals combines two of the Institute's historic and emblematic calls for proposals. It also incorporates three actions from the Ten-year strategy into dedicated sections: 1- action IV.3.6 (human and social sciences and intervention research on determinants and innovative support solutions); 2- action IV.2.2 (human and social sciences and PHIR on care and support for children and adolescents and young adults (AYAs)); 3- action III.1.5 (research in the field of tertiary prevention for cancers with a poor prognosis). The redesign of this call for proposals is in response to a recommendation made by INCa's SAB: to provide the scientific community with greater visibility with respect to calls for proposals in order to reflect national policy in this area.

2023 will see the launch of a new scheme to develop research focusing on the prevention of smoking, which is the leading risk factor for cancer. Following on from the work carried out in the INCa/NCI workshop, aimed at defining priority research questions in this area, a consortium will be created via a call for applications for an integrated cross-disciplinary research programme. The project will be defined in 2023.

Research chairs provide a relevant innovation framework for the development of human and social sciences and public health research related to cancer prevention. The main objective of this scheme is to position research teams in underdeveloped or emerging areas, and to establish partnerships that will ensure their long-term sustainability. Hence, in its new configuration, this five-year programme will benefit from: support from INCa, the financial involvement of the partners, and an agreement in principle from the partner academic bodies to create a position in the field at the end of the five-year period. An Alcohol Chair will be launched in 2023; one of its main areas of focus will be primary prevention and combating inequalities in the area of addiction.

The development of exchanges between researchers and the creation of knowledge-sharing forums are key tools for structuring research in the field of human and social sciences, epidemiology and public health. With regard to the development of PHIR, which is a key priority of the ten-year strategy, symposia on the challenges and methods involved will be organised with the European Public Health Association and the French Association of Applied Psychology. In addition, following on from previous events, INCa will be organising the 6th International French-language symposium on population health intervention research (PHIR), entitled "Intervening, acting with and for citizens, patients, and workers: contributions of intervention research in the field of cancer", on 12 and 13 December 2023 in Paris. The special issue resulting from the 2021 symposium will be published in the journal Psycho-oncologie: the work will be finalised during the course of the year.

Coordination of the network of PhD researchers in human and social sciences, epidemiology and public health will continue, as will the national seminar that brings together all funded PhD students to present their work and build a multidisciplinary scientific community. This seminar will be held on 25 and 26 September 2023.

Turning to psychoactive substances, a symposium on "Young people and psychoactive substances: prevention research perspectives" will be held on 30 March 2023, in partnership with Institut de recherche en santé publique (French Public Health Research Institute), particularly for PHIR. The event will be in hybrid format, with around 100 people attending online and 60 people in-person. In addition, for young researchers who are invested in the field of smoking and alcohol scheme, a symposium to present the results of their research and work in progress will be held on 8 October 2023, bringing together all funded researchers. Supported within the framework of the addiction fund, these events will be attended by both researchers and field practitioners.

Following the European Meetings and the "Cancer & Work" Meetings in 2022, a consortium of European scientists will draw up a White Paper dedicated to the topic of "Cancer & Work". This White Paper will provide European decision-makers with research perspectives in the field of human and social sciences on the subject of returning to work after cancer. Led by INCa in collaboration with the Karolinska Institute, this work will be presented on 9 May 2023 in Sweden to mark the end of the Swedish European Presidency, and handed over to the French Health Minister.

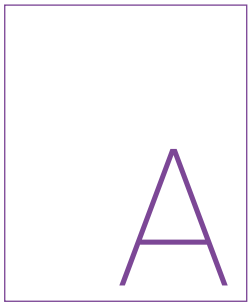
The Ten-Year Cancer Control Strategy makes health promotion aimed at children and adolescents a priority in order to improve prevention.

With this in mind, INCa is organising a French-language scientific symposium on health promotion in schools, along with its partners (Santé Publique France, the General Directorate for Education, the Interministerial drug and addictive behaviour prevention scheme, the University network for health education and the International French-language network for health promotion). This two-day scientific event, to be held on 30 November and 1 December 2023 in Paris, will provide an opportunity to discuss recent and on-going research in France and other countries, as well as to outline prospects for future research.

With regard to the evaluation of research support schemes, following on from the preparatory work carried out in 2020, we will finalise the analysis of projects funded under the call for research proposals in human and social sciences, public health and epidemiology. This will entail the use of an international scientific committee to monitor the analysis work carried out, particularly in terms of identifying the knowledge produced as a result of this call for proposals.

Finally, our analysis of the data obtained from the fourth Cancer Barometer will be completed in 2023. This study is based on the analysis of a telephone survey carried out on a random sample of the French population, the only tool available in France to gauge the beliefs, perceptions, knowledge, opinions and behaviour of the population with regard to cancers, their risk factors, screening and prevention methods. Since these are all guiding factors when it comes to behaviour, it is essential to study them. Produced with the collaboration of Santé Publique France, researchers, stakeholders and user representatives, an eight-chapter book will be published on 4 February 2023, and a press conference will be held. Scientific promotion activities concerning this project will be carried out during the course of the year.

LAUNCH OF AN AMBITIOUS PROGRAMME DEVOTED TO RESEARCH DATA MONITORING TO PRODUCE *EX-ANTE* AND *EX-POST* SCIENTIFIC EVALUATION OF RESEARCH PROGRAMMES



dedicated programme to decipher funding data will be launched. In fact, we need to improve our monitoring over time and along the "impact pathway", in order to produce *ex-ante* and *ex-post* evaluation. The numerous actions that will be carried out should allow us, to meet the objectives included in the Ten-year strategy and the objectives and performance contract (COP), to address the lack of an evaluation strategy as highlighted by the SAB members.

Two areas have been prioritised:

- for retrospective data (since 2008): data recovery scenario will be implemented for all projects (funded or not). The only data currently available and therefore usable at the Institute are sourced from application files submitted to evaluation committees. These data are too imprecise to allow a reliable identification of research outcomes several years after funding. Currently, only returning to the application file allows us to carry out some specific analyses. This tedious and time-consuming work ultimately has no added value for defining proxies enabling ex-post evaluation. Collecting this information via a questionnaire has limitations (~25-30% response rate on average). The most suitable solution, in order to obtain reliable and exhaustive information, is based on the use of the final follow-up report, which includes the information needed to query international databases. These data are not currently available in electronic format. Therefore, several months will be needed to implement a usable ad-hoc database;

- for prospective components from 2025 onwards: an upgrade of our IT system is planned in order to have a structured and interoperable database for administrative and research data (implementation of new electronic follow-up report templates produced by the French research funders working group, integration of interoperable functionality such as ORCID©, etc.).

We also plan to strengthen *ex-ante* evaluations to feed research programming. This will be possible by enhancing the data currently available.

This is a priority cross-cutting project. The Institute must strengthen its control over funding data, and upgrade its IT system in respect of administrative and research data. The implementation of these solutions based on digitisation, interoperability and automation will allow more efficient data processing in the future. These developments are essential to meet the challenges regarding analysis, enhancement and openness of the Institute's portfolio. These pragmatic proposals, based on the principle of "one input – multiple reuse" will make it possible to feed other strategic issues such as the INCa – Open Science Monitor (research programming law target indicator for 2030: 100% of publications resulting from public funding must be accessible). However, this will take time, and requires significant investment in human and financial resources. This programme would also be in line with the 2022 INCa's SAB, the General Inspectorate of Social Affairs (IGAS, Inspection générale des affaires sociales) and the General Inspectorate of Education, Sport and Research (IGSR, Inspection générale de l'éducation, du sport et de la recherche) recommendations[5] (Evaluation of the 2014-2019 Cancer control plan).

5. Ensure the external scientific evaluation of research support programmes by Hcéres prior to a new programme and with a view to their possible development
Plan from the construction of the ten-year cancer control strategy, its external evaluation process and a scientific evaluation schedule by Hcéres for research programmes funded by programme 172
External evaluations will be useful for INCa's International Scientific Advisory Board. Indeed, the law of 8 March 2019 stipulates the need to provide a mid-term review on the relevance of the ten-year cancer strategy

4 Appendices

COMMON SCIENTIFIC OUTLINE

Established in 2000, the International Cancer Research Partnership (ICRP) is a unique alliance of cancer organisations, working together to enhance global collaboration and strategic coordination of cancer research. It includes 150 worldwide organisations from Australia, Canada, France, Japan, the Netherlands, United Kingdom, and the United States. INCa joined this partnership in 2009.

This consortium aims to improve access to information about cancer research being conducted, explore opportunities for cooperation between funding agencies, and enable our members to maximise the impact of their independent efforts.

ICRP organisations share funding information in a common format (known as the Common Scientific Outline or CSO) to facilitate pooling data and evaluating data across organisations.

The Common Scientific Outline, or CSO, is a classification system organised around seven broad areas of scientific interest in cancer research. The development of the CSO is laying a framework to improve coordination among research organisations, making it possible to compare and contrast the research portfolios of public, non-profit, and governmental research agencies. This classification is subdivided in 7 categories:

- Biology
- Aetiology (causes of cancer)
- Prevention
- Early Detection, Diagnosis, and Prognosis
- Treatment
- Cancer Control, Survivorship, and Outcomes Research
- Scientific Model Systems

As a member of the ICRP consortium, INCa and its partners use this classification. The types of research projects funded by INCa, the French Ministry of Health (DGOS) and Inserm for ITMO Cancer-Aviesan that are presented in this report are based on this CSO classification.

THE DIFFERENT CSO CATEGORIES INCLUDE:

- **CSO 1 Biology**
  - **1.1** Normal functioning
  - **1.2** Cancer initiation: alterations in chromosomes
  - **1.3** Cancer initiation: oncogenes and tumour suppressor genes
  - **1.4** Cancer progression and metastasis
  - **1.5** Resources and infrastructure

- **CSO 2 Aetiology**
  - **2.1** Exogenous factors in the origin and cause of cancer
  - **2.2** Endogenous factors in the origin and cause of cancer
  - **2.3** Interactions of genes and/or genetic polymorphisms with exogenous and/or endogenous factors
  - **2.4** Resources and infrastructure related to aetiology

- **CSO 3 Prevention**
  - **3.1** Interventions to prevent cancer: personal behaviours that affect cancer risk
  - **3.2** Nutritional science in cancer prevention
  - **3.3** Chemoprevention
  - **3.4** Vaccines
  - **3.5** Complementary and alternative prevention approaches
  - **3.6** Resources and infrastructure related to prevention

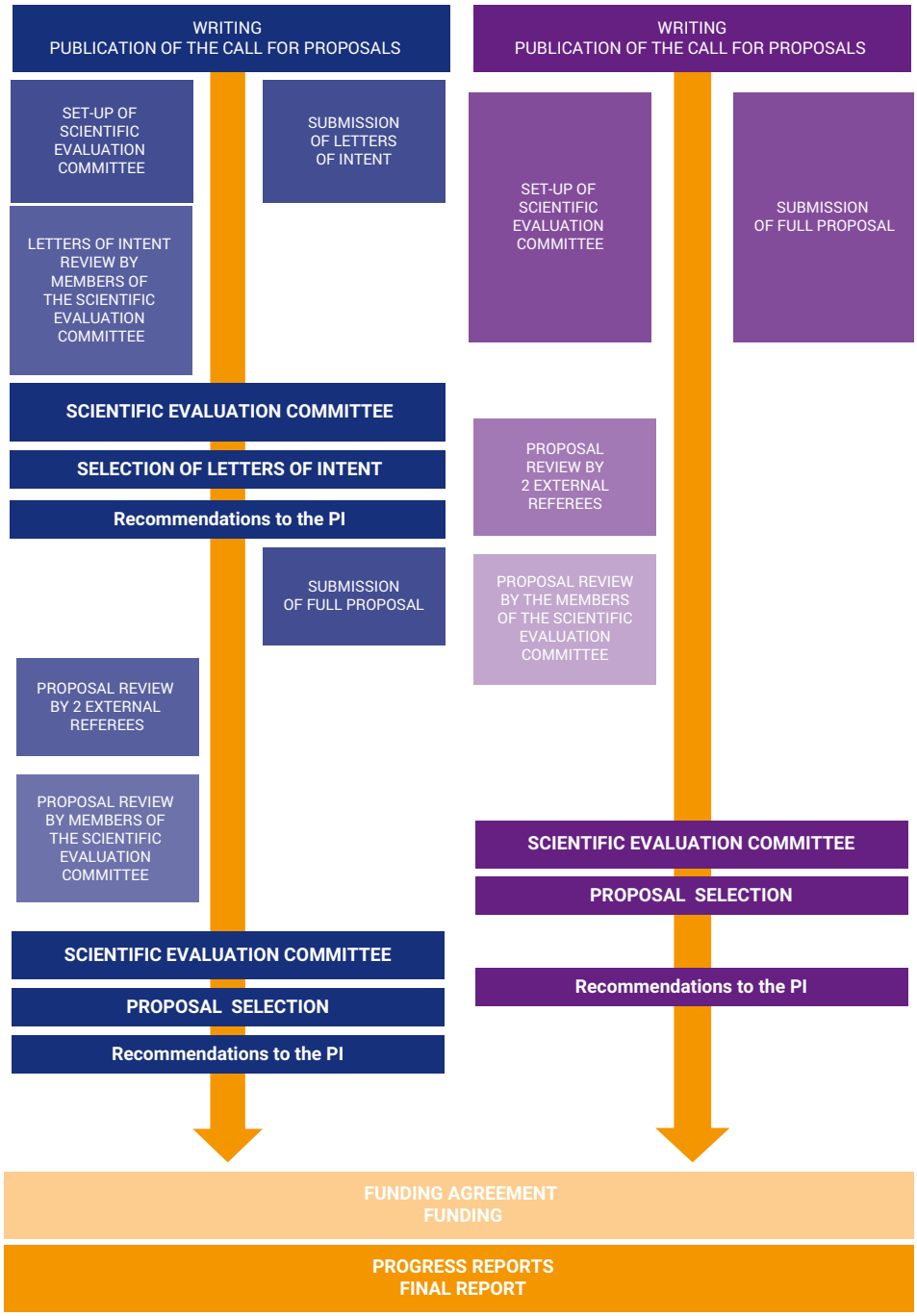
- **CSO 4 Early Detection, Diagnosis, and Prognosis**
  - **4.1** Technology development and/or marker discovery
  - **4.2** Technology and/or marker evaluation with respect to fundamental parameters of method
  - **4.3** Technology and/or marker testing in a clinical setting
  - **4.4** Resources and infrastructure related to detection, diagnosis, or prognosis

- **CSO 5 Treatment**
  - **5.1** Localised therapies – Discovery and development
  - **5.2** Localised therapies – Clinical applications
  - **5.3** Systemic therapies – Discovery anddevelopment
  - **5.4** Systemic therapies – Clinical applications
  - **5.5** Combinations of localised and systemic therapies
  - **5.6** Complementary and alternative treatment approaches
  - **5.7** Resources and infrastructure related totreatment

- **CSO 6 Cancer Control, Survivorship, and Outcomes Research**
  - **6.1** Patient care and survivorship issues
  - **6.2** Surveillance
  - **6.3** Behaviour
  - **6.4** Cost analyses and health care delivery
  - **6.5** Education and communication
  - **6.6** End-of-life care
  - **6.7** Ethics and confidentiality in cancer research
  - **6.8** Complementary and alternative approaches for supportive care of patients and survivors
  - **6.9** Resources and Infrastructure related to cancer control, survivorship, and outcomes research

- **CSO 7 Scientific Model Systems**
  - **7.1** Development and characterisation of model systems
  - **7.2** Application of model systems
  - **7.3** Resources and Infrastructure related to scientific model systems

INCA'S CALLS FOR PROPOSALS: SCIENTIFIC AND OPERATIONAL MANAGEMENT



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