Institut Curie – 26, rue d'Ulm – 75248 Paris Cedex 05 – France – Tel.: +33 (0)1 56 24 55 00

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Annual Report 2021

Curie: Uniting our strengths

institut Curie

CONTENTS

Institut Curie: united in building our future

One hundred years ago, the 'Fondation Curie' was born. At the same time, Marie Curie crossed the Atlantic and returned to France with a precious gram of radium. Symbolically, these two events triggered the starting points of two extraordinary adventures. The first continues to immortalize the action of Institut Curie in terms of its research, care, and teaching thanks to the generosity it receives. The second has opened the way to many scientific discoveries. We can only be grateful to Marie Curie and her successors for their tireless efforts to advancing science, fighting cancer, and helping cure more and more patients.

Since then, through the teams based at its three entities - the Research Center, the Hospital Group and Head Office - Institut Curie has fully embraced these missions bestowed on it by its illustrious founder. The MC[21] strategic plan, which ended in 2021, pursued the objectives of an Institut Curie that is ever more innovative in the face of the challenges posed by cancer. Ever more daring in its scientific choices, and ever more effective in its patient care.

As you read these lines, the thinking behind the launch of Institut Curie into the next decade is fully underway, by extending and accompanying investments made until 2021. All employees have been invited to contribute to the development of this Curie 2030 strategic plan. We would like to thank them for their involvement in this ambitious program, which will consolidate Institut Curie's national and international reputation for excellence in basic research and as an expert center for cancer research. As a European leader in the fight against cancer, this plan commits us to our employees, our patients, our institutional and industrial partners as well as our donors and sponsors. It commits us to making our common future, a future without incurable cancer. ■

Prof. Thierry Philip, Chairman of the Executive Board
Prof. Djillali Annane, member of the Executive Board
Prof. Dominique Deville de Périère, member of the Executive Board
Prof. Alain Puisieux, Director of the Research Center
Prof. Steven Le Gouill, Director of the Hospital Group
Jacques Gilain, Head Office Director

To be at the forefront of research and attract scientific talent

In 2021, Institut Curie celebrated its 100th anniversary and laid the foundations for its future developments. Professor Thierry Philip, Chairman of the Executive Board, and Daniel Thierry, Chairman of the Supervisory Board, discuss the ambition and prospects of this illustrious institution.

What were the highlights of the past year?
Daniel Thierry: The first thing I would like to highlight about 2021, which is still tainted by the health crisis, is the unfailing support of our patrons and donors, our public partners and the strong commitment of all Institut Curie staff. In September 2021, the arrival of Professor Steven Le Gouill as Director of the Hospital Group launched a new dynamic. With the support of Carnot Curie Cancer, two UHR grants (University Hospital Research programs within the health sector: CASSIOPEIA and EpCART) were obtained for a budget of approximately 20 million euros. This is a great accomplishment.

Prof. Thierry Philip: The two UHR grants are, of course, a great source of pride. They reward the work of Institut Curie's medical and research teams and open up new perspectives for the development of future cancer treatments. The appointment of Professor Edith Heard as head of Institut Curie's Scientific Advisory Board is also to be welcomed. Professor at the Collège de France, Director General of the European Molecular Biology Laboratory (EMBL) and former director of a research unit at Institut Curie, this eminent scientist will be able to support our ambitions in a fair and emblematic way.

This year celebrated the foundation's 100th anniversary, what was this like for you? What event marked you the most?
Daniel Thierry: Due to the health situation in France and Europe, we were somewhat bitter about the cancellation of many planned events, especially those that would have allowed us to get together and have our employees contribute more. But we were finally able to follow in Marie Curie's footsteps on a trip to the United States in November. The welcome we received was exemplary. The official figures, both French and American, were very receptive to our approach. They still share our values, those held by Marie Curie 100 years ago! The scientific work of our illustrious founder remains engraved in everyone's memory and is integrated into our daily ambitions!

In this election year, what do you expect from future orientations in the fight against cancer?
Prof. Thierry Philip: The ten-year strategy to fight cancer was announced on 4 February 2021 by the President of the French Republic. Although I am fairly optimistic about the policy implemented by the government in this area, I remain, given our difficulty in keeping the best talent in France, more reserved about the law on research programming. With 0.76% of GDP devoted to research, and 1.44% if we include private funding, France is only ranked 10th among European countries.

Daniel Thierry: Investment in these sectors is a major driver for job creation and economic development, not to mention the potential for innovation and creativity for our country's doctors and researchers!

In this context of strong competition within the world of research, and given that the health crisis has undermined the vocation of healthcare professionals, how does Institut Curie maintain its attractiveness?
Prof. Thierry Philip: This is an ongoing struggle that remains at the forefront of our minds on the Supervisory Board and the Executive Board. While Institut Curie benefits from a certain attractiveness due to its renowned and recognized expertise, its reputation, and its history, we must maintain an attractive salary structure in order to retain the best talent. This deliberation will be at the heart of the social component of the Curie 2030 strategic plan that we launched at the end of 2021.

> "The Curie model is unique, both private and public, which attracts the best doctors and researchers."
>
> **Daniel Thierry,**
> Chairman of the Supervisory Board

What will be the highlights of 2022?
Prof. Thierry Philip: Without a doubt, the accreditation of the Hospital Group by the French National Authority for Health. At the end of the year, the extension of the new Saint-Cloud Hospital will have finished and that will be another highlight! With regards to our various establishments in Paris, we hope that the projects concerning the future Claudius Regaud research building and the extension of the Coursaget hospital can be accelerated. The year 2022 will also be marked by the creation of our new Curie 2030 strategic plan, as we are committed to an open, collective, and collaborative approach. Our objective is to bring Curie 2030 to life, despite a global economic and geopolitical context that remains uncertain.

> "Curie 2030 is the very concept of the Louvre Pyramid: young talents take initiative and carry out innovative projects with a deep respect for our history and our values."
>
> **Prof. Thierry Philip,**
> Chairman of the Executive Board

Daniel Thierry: Our first challenge will be to find the resources to adapt to economic constraints and go beyond these difficulties. The second will be for Institut Curie to look ahead into the decade leading up to 2030. This starts with a governance system in working order. We are now at that point. In March 2021, the Director of the Research Center, Professor Alain Puisieux, presented his six-year program to maintain the Research Center, at the forefront of international research. In 2022, Professor Steven Le Gouill will present his vision for the future of the Hospital Group. The objective is also ambitious: to ensure that Institut Curie is a world leader in cancer research. Armed with these two strong intentions and a Curie 2030 strategic plan supported by all the staff, Institut Curie can confidently enter its second centenary. ■

One hundred years later, our ambition remains intact: gain understanding to treat and cure more and more patients

Institut Curie is made up of three entities that work hand in hand and share the same humanistic desire to progress in the fight against cancer. A group interview with Professor Alain Puisieux, Director of the Research Center, Professor Steven Le Gouill, Director of the Hospital Group, and Jacques Gilain, Director of the Head Office.

What were the highlights for Institut Curie in 2021? How will they drive research and help in the fight against cancer?

Prof. Alain Puisieux: I would like to highlight the progress made in our scientific program on our three sites. Whether in Paris, Orsay or Saint-Cloud, we have laid the foundations for several key projects for the future of the institute and strengthened our ties with the teams at the Hospital Group. I would like to emphasize the exceptional quality of the work carried out by our research teams. This is demonstrated by the 536 scientific publications in leading international journals and numerous national and international tenders. Since 2007, the ERC (European Research Council) grants obtained by our researchers represent nearly 10% of French ERC grants in the field of life sciences.

Prof. Steven Le Gouill: University hospital research is at the heart of the Curie model, and the two UHR grants obtained at the end of the year illustrate our expertise in this area, as well as the seven hospital clinical research programs funded by the French Ministry of Health. Our independent review of excellency, the renewed momentum in clinical trials and our publications in the leading international journals reflect our ability to interact with our counterparts and the attractiveness of Institut Curie.

Jacques Gilain: In terms of innovation, 2021 was a very positive year. The strength and relevance of the model supported by Institut Curie contributed to exceptional fundraising results for the development of start-ups. We also celebrated the tenth anniversary of our Carnot Label, which facilitates the establishment of industrial partnerships. Finally, we have developed cross-functionality between the three entities. Institut Curie's excellence is rooted in our teamwork.

However, 2021 has not been easy. Particularly because of the pandemic. What challenges have you had to overcome to maintain your high standards?

Prof. Steven Le Gouill: Institut Curie's carers and doctors were not spared the difficulties seen by the pandemic. Perhaps they have been affected even more so because they have been forced to adapt to continue making excellence a priority. I would like to pay tribute to the courage seen by all the teams who responded. They showed resilience and significant professionalism to ensure that their missions were carried out.

Prof. Alain Puisieux: Research is by nature a group effort, based on the exchange of ideas and skills. Distancing has created a gap, particularly in terms of scientific leadership. One of our main challenges was to ensure that the scientific project and the real estate project were consistent, by working hand in hand with the departments at Head Office: our work tool must be as efficient as possible. This is necessary to be competitive at an international level.

Jacques Gilain: During the pandemic, we took up three major challenges: maintaining donor trust and increasing the funds collected; managing the teams at Head Office in a context of teleworking and partial activity; and developing our ideas on how to manage the clinical translational research and innovation project. The latter is a project that aims to strengthen the coherence of our work and make our processes more fluid.

2021 was also the year of the Foundation's 100-year anniversary. What did you take away from this?

Jacques Gilain: This anniversary marks our institution's ability to be a long-term player. It also brings to light the trust that binds us to our donors and patrons, who have accompanied us for 100 years in all our projects.

Prof. Alain Puisieux: We have experienced some emotionally and symbolically powerful moments, particularly during the trip to the United States in November 2021. This celebration highlighted the importance of our values and the strength of Marie Curie's vision, which still drives us today: fundamental research that feeds therapeutic innovation for the benefit of patients and humanity as a whole.

Prof. Steven Le Gouill: The name Marie Curie remains synonymous with scientific innovation and a pioneering spirit, and the reputation of Institut Curie stretches far beyond France. We are opening a second centenary, which we must imagine in terms of research, care, and the patient's journey.

The year 2022 will be marked by the development of the Curie 2030 strategic plan. What do you expect from this project for Institut Curie and for your teams? What qualities does Institut Curie have to achieve this?

Prof. Alain Puisieux: We are going to make the strategic plan a growth-generating steering tool in terms of research competitiveness, therapeutic innovation, and digital transformation. Not forgetting the social and corporate social responsibility aspects, which are essential in attracting and retaining talent. We must not forget that Institut Curie is, above all, a human adventure and our main asset is our staff.

Jacques Gilain: To design this strategic plan, we initiated a participatory approach that gives specific importance to employees. More than a hundred of them will be directly or indirectly involved in writing it.

Prof. Steven Le Gouill: Curie 2030 is the foundation stone for yet another 100 years of Institut Curie's history. We have a role to play in making our voice heard at both a European and French level in our fields of expertise, particularly regarding the younger generations. ■

"FONDATION CURIE: 100 YEARS OF GENEROSITY IN THE FIGHT AGAINST CANCER"

Filmed at the Musée Curie (Curie Museum). This program launched the Fondation Curie's 100-year celebrations on 27 May 2021.

GALA DINNER

A gala dinner was organized on 9 November 2021 at the Harvard Club in New York, under the presidency of Mrs. Christine Schwarzman, producer and philanthropist, and Dr. Susan Blumenthal, Assistant Secretary of Health for four American presidents, and in the presence of numerous personalities.

A double centenary at Institut Curie in 2021

In 2021, Institut Curie celebrated its one hundredth anniversary since the creation of its foundation. A foundation that is recognized as being of public interest. This was an opportunity to remember that since the very beginning, the role of generosity has been essential in carrying out its research, care, and teaching missions.

In parallel with this anniversary, Institut Curie also commemorated Marie Curie's triumphant trip to the United States in 1921. On 8 November 2021, a delegation of Institut Curie officials, scientists and doctors visited the French Embassy in Washington, D.C. (United States). This memorial and scientific event entitled "in the footsteps of Marie Curie" allowed for an unprecedented and historic meeting between the descendants of Marie Curie and the great-great-granddaughter of Marie Mattingly Meloney.

In 1921, this feminist figure had made it possible to collect one million dollars from American women, the sum needed to buy a gram of radium. This was a valuable gift for the continuation of Marie Curie's work.

AT THE FRENCH EMBASSY IN THE UNITED STATES

1/ From left to right, Prof. Thierry Philip, Chairman of the Executive Board, Prof. Dominique Deville de Périère (member of the Executive Board), Daniel Thierry, Chairman of the Supervisory Board, Prof. Djillali Annane (member of the Executive Board), Prof. Alain Puisieux, Director of the Research Center and Prof. Steven Le Gouill, Director of the Hospital Group.

2/ From left to right, Raphaël Rodriguez, head of the Chemical Biology team, Kethevane Gorjestani, the moderator of the round table, Dr. Sarah Watson, medical oncologist and researcher, and Fatima Mechta-Grigoriou, head of the Stress and cancer team.

3/ From left to right, Sean Meloney Harrison, descendant of Marie Mattingly Meloney, and Marie Curie's great-grandsons, Marc Joliot, and Yves Langevin.

RESEARCH

Two UHR grant winning projects

Two large-scale projects, led by Institut Curie, have won the "University Hospital Research" (UHR) program for health grant. Their objective: to respond to the therapeutic impasse of certain cancers. Bringing together academic, hospital and industrial partners, each of these projects will benefit from almost 10 million euros over a five-year period.

- CASSIOPEIA, directed by Fatima Mechta-Grigoriou, principal investigator of the project, head of the Stress and Cancer team and deputy director of the Inserm U830 unit, and Prof. François-Clément Bidard, medical oncology researcher, head of the Translational Research Group Circulating Tumor Biomarkers, in collaboration with several major industrial partners (Institut Roche, Roche, Oncodesign). This project aims to study triple-negative breast cancer, which affects 15% of breast cancer patients and for which there is an urgent need for innovative treatments and early detection of relapses. The long-term ambition is to develop novel therapies targeting fibroblasts, a cell type that is very abundant in tumors and has not been targeted for treatment until now.
- EpCART, led by Prof. Sebastian Amigorena, principal investigator of the project and head of the Immune Responses and Cancer team (Inserm U932), and Dr. Marion Alcantara, a hematologist in charge of the cell therapy program, will combine the latest knowledge in immunology and epigenetics from its laboratories: - the modulation of gene expression that does not involve DNA mutations - with CAR-T therapies. Knowledge gained by research carried out by Institut Curie and developed by the biotech company Mnemo Therapeutics. This project also involves the MEARY cell and gene therapy center at the AP-HP (Public Assistance - Paris Hospitals). After the preclinical validation of this unique approach, a clinical trial will evaluate the feasibility of producing these original cell therapies and the absence of side effects in patients with solid tumors.

PUBLICATION

The pathogenic role of retrotransposons deciphered

The Epigenetic Decisions and Reproduction team (CNRS UMR3215/Inserm U934/Sorbonne University), led by Deborah Bourc'his, published in Nature on 13 January 2021 the results of its work on a new defense system, exploring the multiple ways in which retrotransposons (mobile genetic entities capable of moving and 'jumping' around the genome) can cause pathologies. This work suggests that methylation defects in retrotransposon RNAs may contribute to diseases such as cancer, autoimmune diseases, and neurodegenerative diseases.

Nature 2021, Chelmicki and al.

RENEWAL OF FRAMEWORK AGREEMENTS WITH CNRS AND INSERM

After two years of collective work by Institut Curie's Research Center teams and Head Office, the framework agreements with the CNRS and Inserm were renewed and signed in January 2021. They provide a framework for the relationship between Institut Curie and these national public institutions, which employ nearly 25% of the Research Center's staff and contribute to the funding of the 13 mixed research units. The renewal of these agreements was an opportunity to clarify and formalize their content, so that they reflect the practices within the units.

IMMUNOTHERAPY

A new molecule improves survival in uveal melanoma cases

An international randomized phase 3 study, coordinated in France by Dr. Sophie Piperno-Neumann, medical oncologist at Institut Curie, demonstrates the efficacy of a brand-new immunotherapy molecule, tebentafusp, on the overall survival of patients with HLA A2 positive metastatic uveal melanoma. It is the first bispecific and much-awaited survival enhancer in oncology for this rare melanoma.

New England Journal of Medicine 2021, Nathan and al.

INTERNATIONAL

INSTITUT CURIE IN TANZANIA: THE CO-PILOT OF A COMMITTED PROJECT TO FIGHT CANCER

In December 2021, a delegation from Institut Curie, led by Prof. Thierry Philip, Chairman of the Executive Board, travelled to Tanzania to support and meet the partners of the Tanzania Comprehensive Cancer Project (TCCP) financed by AFD. The objective of this 4-year project is to reduce cancer mortality rates through a unique public-private collaboration involving Tanzanian public health institutions and the Aga Khan Foundation's care centers. As advisor and co-leader of the TCCP, Institut Curie is bringing its experts in radiotherapy, pathology, palliative care, nutrition, physical activity, and research, and is working with Tanzanian specialists to raise awareness of cancer screening on the ground.

AWARD

NICOLAS SERVANT, SUZIE URCEL AND CLAIRE SNIEHOTTA, WINNERS OF THE PRIX CURIE 2021

"Receiving the Prix Curie is a great source of pride. In the age of big data and precision medicine, this prize provides recognition of our bioinformatics support work for research and care in oncology." **Nicolas Servant** is co-director of the Research Center's bioinformatics platform in Paris. He joined Institut Curie in 2005. His team provides technical and scientific support in data analysis, innovation, and bioinformatics.

"For me, this Prix Curie is a recognition of my unwavering commitment to the institute. It is a strong signal to caregivers in these difficult times. I am truly proud to belong to the great Curie family." In 2008, **Suzie Urcel** (in the middle) joined the operating room of the Saint-Cloud Hospital Group as a nurse anesthetist, in charge of emergency trolleys and intra-hospital vital emergencies. She is also a health simulation trainer and an emergency care trainer (AFGSU: Certificate of Training in Emergency First-Aid).

"This award is first of all a nice surprise! It highlights the generosity of our loyal donors who have supported Institut Curie's missions since its creation." **Claire Sniehotta** (right) is a marketing manager in the Donor Relations Department at the Paris Head Office. Since 2010, she has been involved in defining, implementing, and steering the marketing strategy with the aim of developing resources from private generosity.

INNOVATION

28 start-ups have been created at Institut Curie since 2002, including 12 in the last five years. More than 525 million euros of funds have been raised. Five years after the initiation of the new strategy for valorization and industrial partnerships, Institut Curie is now identified as a leading center at European level capable of transforming innovation into entrepreneurial success. With its integrated start-up incubation program, presented for the first time in 2021, Institut Curie is continuing its drive to accelerate innovations in cancer research.

DATA

Institut Curie, founding member of DIGICORE

In Brussels in April 2021, Institut Curie signed the deed to create DIGICORE (European Digital Institute for Cancer Outcomes Research). This European Economic Interest Grouping (EEIG) aims to meet the scientific, regulatory, and commercial challenges of so-called real-life data. This information, generated and collected during routine care or via connected objects over the course of a patient's daily routine, makes it possible to optimize research and treatment and to improve care paths. Recognized as an expert center in France and Europe in the management and use of this data, Institut Curie was heavily involved in the creation of this alliance, alongside some thirty European cancer centers and private players.

REAL ESTATE PROJECT

AN AMBITIOUS PLAN: THE DEVELOPMENT OF INSTITUT CURIE CONTINUES

Institut Curie's building and renovation program, a priority of the MC21 Plan, covers the key issues we face to meet the challenges of cancer research, ensures quality patient care, and promotes its attractiveness. After various revisions, the last of which took place in mid-2021, 190.9 million euros will be invested in the long run. The extension and renovation of the current Saint-Cloud hospital remains the largest project (148 beds and patient areas spread over 25,000 m², including 14,000 m² of new construction, a clinical investigation center and 1,500 m² of research space). In Paris, the new building for the «Coursaget» hospital extension will increase and improve the reception of patients and offer optimal working conditions for the teams. On the research side, the Claudius Regaud extension and the renovation of the Pasteur pavilion will provide 1,500 m² of laboratory space and a space dedicated to support functions.

FUNDRAISING

An exceptional auction at the Hospices de Beaune

The 161st Hospices de Beaune wine auction took place on Sunday 21 November 2021. A record bid for a charity wine lot, a Corton Renardes Grands Cru 2021, was auctioned with half of the proceeds going to benefit Institut Curie. This is the second time Institut Curie has benefitted from this prestigious operation. Pio Marmaï, Institut Curie's patron, worked hard to raise the bids, which reached a record sum of 800,000 euros. Thanks to this collection, Institut Curie will be able to acquire a state-of-the-art microscope equipped with a sampling mechanism that will allow researchers to better characterize tumor cells.

RADIOTHERAPY

Stereotaxis, the future reference treatment for the prostate

The radiotherapy department at Institut Curie, headed by Prof. Gilles Créhange, now routinely offers stereotaxy for certain forms of localized or metastatic prostate cancer, for patients over 70 years of age or with comorbidities.
Stereotaxy is a «concentrated» radiotherapy that takes place over just five sessions spread over a week and a half, which corresponds to a total dose equivalent to a conventional two-month treatment. This technique is very promising, particularly because of very moderate side effects for patients, and could be offered for all patients in the near future.

Institut Curie

3,736
EMPLOYEES

435.6 MILLION €
OF RESOURCES
(source: use of resources statement)

Amount raised
from public donations

31.1 MILLION €
(gifts and sponsorship)

26.7 MILLION €
(bequests and donations)

242,000
ACTIVE DONORS

Labelled Comprehensive Cancer Center since 2018 by the OECI

740
PATENTS

28th
start-up
created in 2021

13.2 MILLION €
of total revenue generated

1st

European Center
for breast cancer care

French cancer
center by number
of patients treated

French cancer
research center

The Research Center

6 thematic areas of research:

- Epigenetics, RNA, and genome dynamics
- Cell biology and developmental biology
- Tumor biology and immunology
- Radiobiology and molecular imaging
- Physics of living systems and chemical biology
- Computational biology and systems biology

1,225
EMPLOYEES
including **74** foreign employees

308
PhD students
including **130** foreign PhD students (42%)

230
postdocs
including **157** foreign postdocs (68%)

87
RESEARCH TEAMS
including **24** junior teams

536
SCIENTIFIC PUBLICATIONS AT THE RESEARCH CENTER

of which, **32.6%** with an impact factor **> 10** (**+20%** compared to 2020)

of which, **7.46%** with an impact factor **> 20**

40.2 MILLION €
IN RESEARCH CONTRACTS

20
ERC GRANTS
(**55** since the creation of these highly competitive funds) including **1** advanced ERC obtained in 2021

9 new emerging and growth-generating programs, including **5** scientific and **4** medical and scientific programs.

13 mixed research units affiliated with the CNRS and/or Inserm and/or university

4 SiRIC labelled research teams

19
technology platforms

The Hospital Group

2,219
EMPLOYEES

377 state-qualified nurses
(operating theatre nurses, anaesthesia nurses, experts, maternity nurses)
102 nursing assistants
386 doctors (including 4 MCU-PH and 15 PU-PH)

97 nursing students and nurses
71 interns

52,691
PATIENTS, including:
13,556 new patients
286 international patients
17,236 patients underoing treatment
(**74%** women and **26%** men)

104,235
CONSULTATIONS

178,939
HOSPITAL STAYS, including:
167,425 outpatient stays (including **60,462** stays in the Day Clinic) and
11,514 conventional hospital stays
4.5 days (average length of stay)

49,124
CHEMICAL THERAPY TREATMENTS performed

14,664
SURGERY HOSPITAL STAYS
including **8,600** outpatient surgery stays

106,963
RADIOTHERAPY sessions

871
SCIENTIFIC PUBLICATIONS FROM THE HOSPITAL GROUP

of which **22.7%** with an impact factor of > 10

of which **8.7%** with an impact factor of > 20

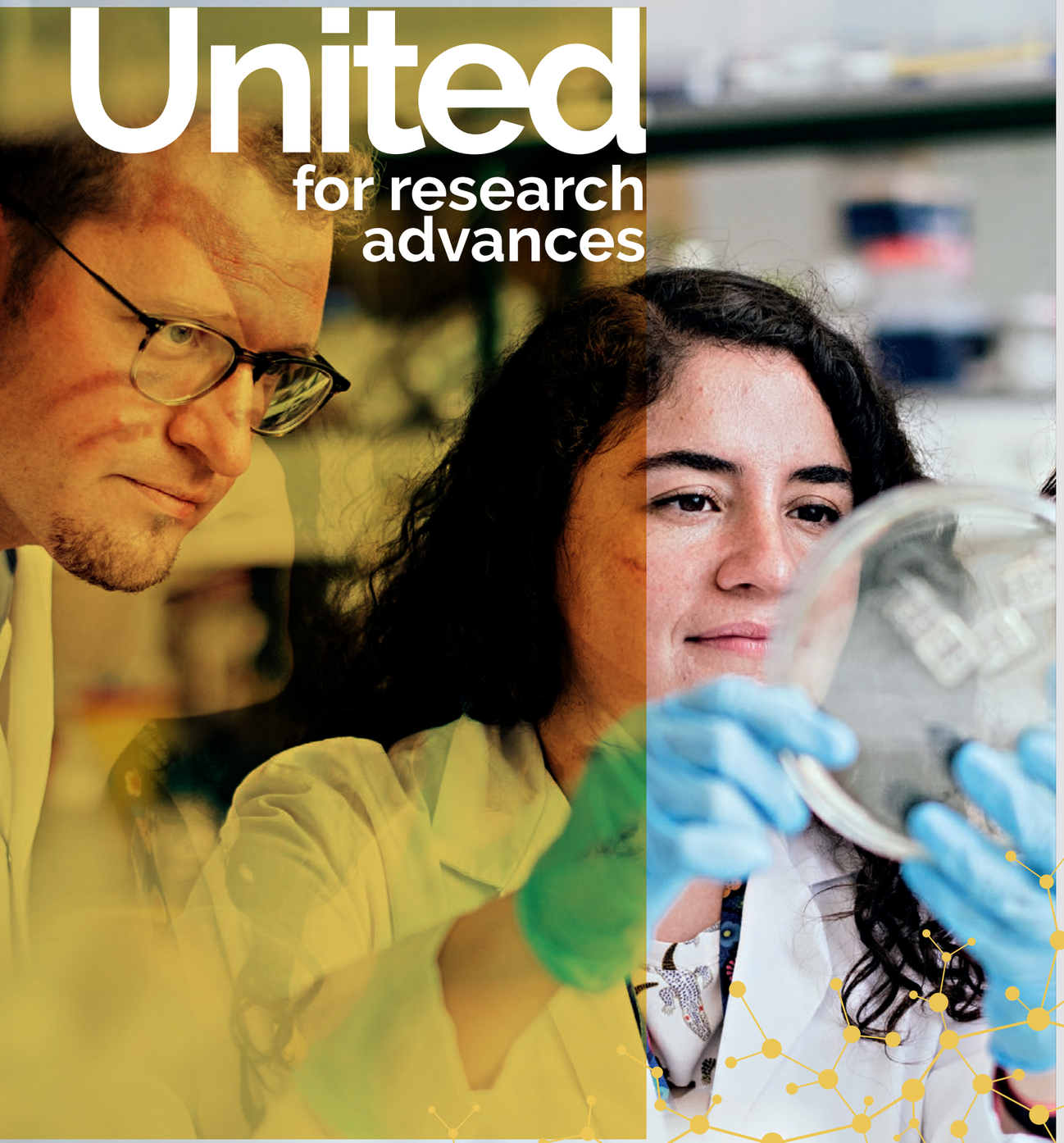
Including **12** A+ and **229** A ranked publications

Number of patients treated

for each type of cancer or tumors at Institut Curie Hospital Group

17,236
patients undergoing treatment, including
74% women
and **26%** men

- **7,476** for breast cancer
- **1,141** for respiratory system cancer
- **1,070** for gynecological cancer
- **851** for cancer of the male reproductive system
- **840** for digestive cancer
- **743** for an eye tumor
- **699** for blood or bone marrow cancer
- **563** for a pediatric tumor
- **508** for skin cancer
- **487** for ENT cancer
- **412** for a sarcoma or complex tumor
- **156** for thyroid cancer
- **99** for urinary tract cancer
- **80** for central nervous system cancer



United for research advances

NEW TREATMENTS

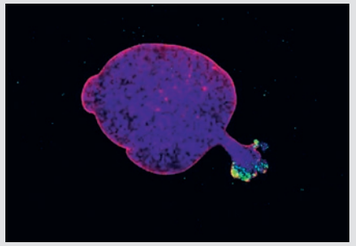
A TEAM DECIPHERS IRON METABOLISM

The work carried out by the Chemical Biology of Cancer team (CNRS UMR3666 / Inserm U1143), led by Raphaël Rodriguez, has revealed a new entry point for inducing death to cells with metastatic potential in connection with iron metabolism. In 2020, this team revealed specific iron-related mechanisms capable of 'reprogramming' certain cells, making them metastatic and resistant to conventional treatments. The researchers then sought to better understand the cell death process of ferroptosis to identify new biomarkers and develop innovative cancer therapies. Raphaël Rodriguez, together with other scientists, Marcus Conrad (a ferroptosis pioneer) and Stuart Schreiber (the founder of modern chemical biology) has published an article that conceptualizes new therapeutic approaches.

Molecular Cell 2021, Rodriguez and al.

CELLS

TREX1 ENZYME IDENTIFIED AS AN AGGRAVATING FACTOR OF BREAST CANCER



Matthieu Piel, head of the Systemic Cell Biology of Polarity and Division team (CNRS UMR144 / Sorbonne University), Nicolas Manel, head of the Innate Immunity team (Inserm U932) and Philippe Chavrier, head of the Membrane and Cytoskeleton Dynamics team (CNRS UMR144 / Sorbonne University), in collaboration with the ENS, PSL, Sorbonne University and the Cordeliers Research Center, are studying the consequences of nucleus ruptures induced by the compression of tumor cells on breast cancer. The nucleus of a cell can be deformed, or even temporarily fractured, if the cell is itself compressed and deformed, for example in the event of migration or proliferation, which then leads to damage to the DNA. The scientists found that the breaks in the nucleus caused by cell compression allow the DNA to encounter the TREX1 enzyme, which makes the cancer cells more invasive and facilitates their spread. The researchers now want to identify and test molecules that could block its activity, inhibitors that could have many applications in therapy.

Cell 2021, Pedreira de Freitas Nader and al.

NEW TEAMS

INSTITUT CURIE PROMOTES YOUNG TALENT

Two new JPIs (junior principal investigators) have recently joined Institut Curie's research teams.

Annabelle Ballesta, mathematician, has taken over as head of the Applied Systems Pharmacology for Cancer team (Inserm U900 / Mines Paris-PSL). *"My team, made up of mathematicians, bioinformaticians and statisticians, aims to optimize and personalize cancer therapies. Our work is based on two axes: the first consists of individualizing drug combinations according to the profile of the tumors. The second is to adapt the administration schedules over 24 hours - we call it chronotherapy - according to different patient parameters such as gender or chronotype, which corresponds to a person's day/night rhythm."*

Enzo Poirier, a virologist by training, heads the new Stem Cell Immunity team (Inserm U932). His mission? To work on the defense programs that preserve the integrity of stem cells, including when confronted with viruses, a largely unexplored field of research in which certain mechanisms are also mobilized by cancer cells. This fundamental work could help identify new therapeutic approaches. *"It is a real opportunity to be able to create a research team at Institut Curie! In addition to the cutting-edge technical facilities available to researchers, I will also take advantage of the Curie environment to ask new questions at the interface between oncology and virology, by establishing collaborations."*

A FACTOR IN MALE SUB-FERTILITY IDENTIFIED

Reprinted with permission from the AAAS

One of the possible origins of male infertility has just been identified by Carsten Janke's team (CNRS UMR3348 / Université Paris Saclay) in collaboration with researchers from two Max Planck Institutes in Dresden and Bonn in Germany, and from the Institut Cochin in Paris. They demonstrated that the loss of a particular enzymatic modification (glycylation) of a protein making up the cytoskeleton fibers called microtubules, leads to subfertility in mice. Having found that in the absence of glycylation, sperm motility is impaired, the researchers used cryo-electron microscopy to visualize the molecular structure of the flagellum and its molecular motors - dyneins. They found that glycylation is essential for coordinating these motors, which is required to keep the sperm swimming in a straight line. Sperm that lack this glycylation step on the microtubules still swam - but mostly in a circle, which prevented them from finding the oocyte to be fertilized. The same defect that causes subfertility in mice could translate into male infertility.

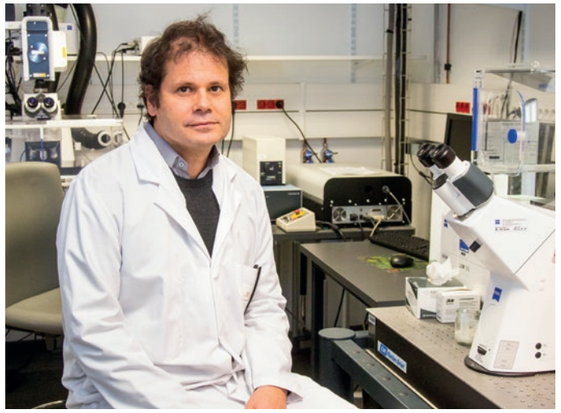
Science 2021, Gadadhar and al.

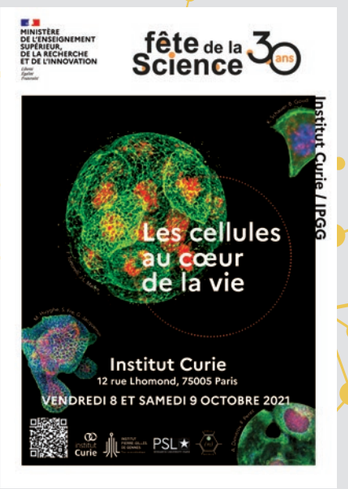
FUNDING

YOHANNS BELLAÏCHE RECEIVES ERC FUNDING

The Polarity, Division and Morphogenesis team (CNRS UMR3215 / Inserm U934 / PSL / Sorbonne University), led by Yohanns Bellaïche(1), is working to better understand the mechanisms that allow tissues to acquire a given shape during their development. Yohanns Bellaïche won funding from the European Research Council (ERC) in May 2021 for the Scalling Sensitivity project. This project will benefit from an ERC Advanced Grant of €2 million over 60 months to understand the links between cell size and tissue shape. This is a real achievement, one that should not be overlooked, given the selective nature of European funding.

(1) Yohanns Bellaïche is also Deputy Director of the Genetics and Developmental Biology unit at the Institut Curie Research Center.





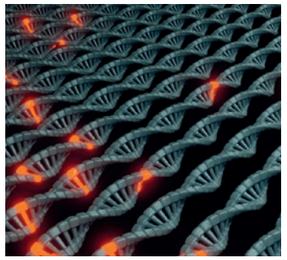
EVENT

Science festival 2021: all mobilised

Around fifty researchers, engineers, post-doctoral students, doctoral students and collaborators from the Physics and Chemistry Curie unit (CNRS UMR168 / Sorbonne University), the Cell Biology and Cancer unit (CNRS UMR144 / Sorbonne University) and the LabEx Cell(n)Scale unit at the Research Center were mobilized to welcome visitors to the 30th edition of the science festival, on 8 and 9 October 2021. Visits to the workshops were offered in the Paris based laboratories of Institut Curie and at Institut Pierre-Gilles de Gennes. With the help of demonstrations, observations, experiments, and posters, young and old alike were able to discover the research carried out at Institut Curie on the theme of «Cells at the heart of life».

GENOME

Optical replication mapping: a new method



A brand-new method for replication by optical mapping, a high-throughput single-molecule approach, has just been developed by the Replication and Genome Instability Program team (CNRS UMR3244 / Sorbonne University), led by Chunlong Chen as part of an international collaboration. Replication is the biological process that allows, at chromosomal level, the identical production of new DNA molecules at each cell division. Proper replication is essential to maintain the integrity of the genome. Researchers are now able to visualizes the sites of replication initiation with great precision and reliability. These results open up prospects for a better understanding of the pathological phenomena (in particular cancers) that can occur when the replication process malfunctions.

Molecular Cell 2021, Wang and al.

COVID 19

The anti-infective power of extracellular vesicles demonstrated

The surface of the SARS-CoV-2 virus, which causes Covid-19, is coated with a Spike protein, which binds to the ACE2 (angiotensin-converting enzyme 2) receptor on the surface of human cells, particularly lung cells, to enter cells. Another membrane receptor on the surface of host cells, the TMPRSS2 (transmembrane protease serine 2) receptor, converts the Spike protein, allowing the virus to enter the cell. The Extracellular Vesicles, Immune Responses and Cancer team (Inserm U932) led by Clotilde Théry, in collaboration with the CNRS and Institut Pasteur, has demonstrated the anti-infectious power of these extracellular vesicles in vitro. These results reveal a therapeutic avenue for the local treatment of Covid-19 which remains to be explored and confirmed by feasibility and efficacy studies.

The Journal of Extracellular Vesicles 2021, Cocozza and al

TECHNOLOGY

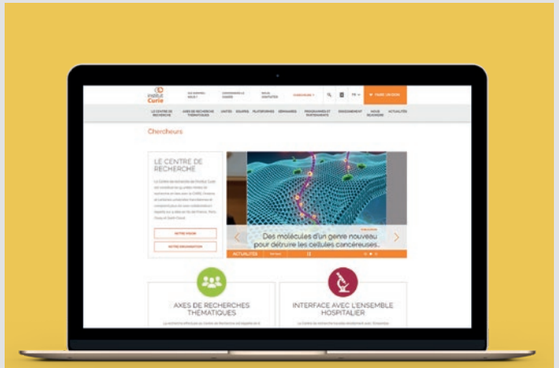
Creation of the CurieCoreTech platform - Extracellular vesicles

In June 2021, Coralie Guérin, manager of the Curie CoreTech Cytometry platform, and Clotilde Théry, head of the Extracellular Vesicles, Immune Responses and Cancer team (Inserm U932), created the Extracellular Vesicles Platform at the Institut Curie Research Center. The platform offers its expertise in the isolation and characterization of extracellular vesicles (exosomes, ectosomes, micro vesicles), following the experimental recommendations published by the International Society for Extracellular Vesicles (ISEV), the «MISEV guidelines». This platform can provide scientific or technical advice, project coordination or training as required.

SINGLE CELL

Four platforms join forces

The Single Cell Initiative is the result of a project proposed by four technology platforms at Institut Curie's CurieCore Tech: Custom Single Cell Omics, High Throughput Sequencing-ICGEX, Cytometry and Bioinformatics (CUBIC). It is part of the Research Center's strategic plan to provide researchers with the most efficient and state-of-the-art tools. The initiative aims to optimize the services and developments of Single Cell technologies for the benefit of the scientific community. One of the technologies recently released by the Custom Single Cell Omics platform is Smart-seq3 technology, a unique scRNA-seq method that covers the entirety of RNAs, allowing allele resolution, splice isoform identification and genetic variants.



SCIENCE AT ITS BEST: A NEW DEDICATED SPACE ON CURIE.FR

Following a collaborative effort, the website **www.curie.fr** now has a new, more modern, and more ergonomic «researchers» area since December 2021. The aim of this thematic space dedicated to the scientific activities of Institut Curie is to better promote the work and teams of the Research Center. With the help of all the researchers, more than 280 pages in French and in English have been updated or created, making it possible to understand the organization of the Research Center, to improve its visibility and to increase its audience within the national and international scientific community.

APPOINTMENT

Handover takes place in the Immunity and Cancer unit

Ana-Maria Lennon-Duménil, an immunologist, has been the head of the Research Center's Immunity and Cancer unit (Inserm U932) since 1 April 2021, succeeding Prof. Sebastian Amigorena, who headed this unit for 12 years. With her Spatio-temporal Dynamics of Immune cells team and in collaboration with other scientists at the Research Center, her work focuses on the use of multidisciplinary approaches to understand, at different scales, the functioning of immune cells.

"My objective is to maintain and even strengthen the diversity of our work in fundamental and translational research. I want our knowledge in quantitative biology, physics, and cellular immunology to reach the patient's bed. The richness of this unit lies in the diversity of the profession and expertise of each person. I must ensure that there is room to talk for all those who contribute, at all different levels, to ensure the smooth running of the unit and its scientific production; indeed, this integrative spirit can only be beneficial to the research we carry out."

Ana-Maria Lennon-Duménil,
Director of the Immunity and Cancer unit

Handover takes place in the chemistry and modelling for cancer biology unit

Florence Mahuteau-Betzer has been appointed as director of the Chemistry and Modelling for Cancer Biology unit (CNRS UMR9187 / Inserm U1196 / Université Paris-Saclay) based in Orsay. This unit is interested in small molecules that disrupt life. The objective of the 40 people who make up the unit is to design and synthesize molecules and study their interactions with biomolecules, mainly nucleic acids, and proteins. Two teams are developing ligands (molecules capable of reversible binding) of particular nucleic acid structures, while the third team is interested in protein ligands, particularly kinases.

"I am very attached to interdisciplinarity, which is important in the understanding of the interactions between small molecules and biomolecules. Our unit brings together strong expertise in each discipline: organic chemists but also biochemists, biologists, modelers, and a doctor, who all work together. The unit also continues to develop innovative methodological tools, which are essential for developing research at the chemical-biology interface."

Florence Mahuteau-Betzer,
Director of the Chemistry
and Modelling for Biology of Cancer unit

United for teaching

21
cross-cutting skills courses in webinar format

140
applications for internships by foreign doctors in 2021

551
PARTICIPANTS
in international courses

59
NEW DOCTORANTS
arrived in 2021

The transmission of knowledge is a necessity required to maintain the level of excellence in medicine and research. Despite the cancellation or postponement of certain training courses due to the Covid pandemic, the Advanced Training Office was able to quickly adapt its activities by changing its delivery methods and developing numerous online courses.

The Advanced Training Office at the Research Center has continued to recruit doctoral students and has not hesitated to set up more courses in 2021, despite the pandemic. *"Many online courses have been developed to support young researchers during this difficult period,"* says Graça Raposo, Director of Advanced Training Office (Research Center). *"Training activities have also been launched in close collaboration with the doctoral students' association, ADIC."*

The online recruitment model set up for the international programs enabled 11 new international PhD students to join Institut Curie. A one-month integration period was offered with specific training for newcomers, which some of them were able to attend even though their arrival was delayed due to the pandemic. They were also able to follow the 21 cross-cutting skills courses and the two scientific integrity courses organized and provided in the form of webinars, along with all the doctoral students.

In the same way, the international courses given by the Hospital Group were resumed in a hybrid format. *"These clinical-biological courses, which are characteristic of Institut Curie's training offer and are open to doctoral students, were once again a great success in 2021,"* explains Prof. François Doz, Director of Advanced Training Office (Hospital Group). *"For example, a course on childhood brain tumors, organized jointly with partners from the Île-de-France region (Université Paris Cité, Necker and Sainte-Anne Hospitals, Gustave Roussy), attracted more than 200 participants and speakers from all over the world."*

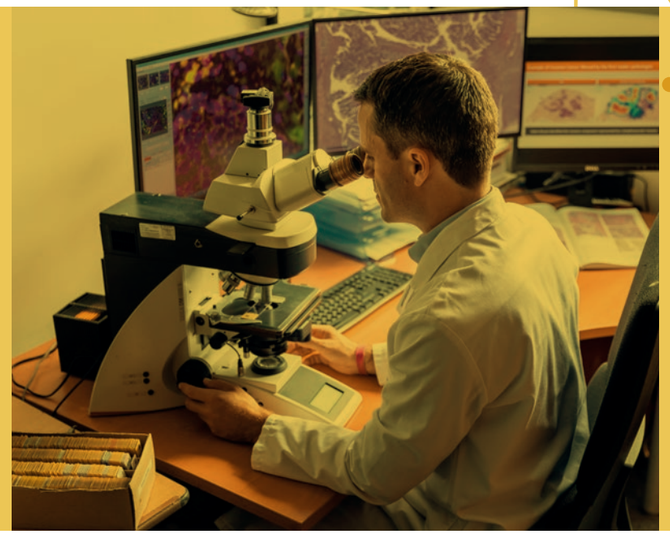
Regular activities, such as courses given to medical students and interns, alternated between face-to-face and distance learning. Online training was organized with university partners and on site at Institut Curie for medical students or students taking university (UD) or inter-university (IUD) diplomas. The second-year masters PhD program for doctors, pharmacists and other healthcare professionals was continued in 2021: it enabled ten doctors, interns, or assistants, working in the fields of cancerology, to be supported following their wish to receive additional training through research in the laboratories of Institut Curie's Research Center. The Hospital Group has also adapted to take over the organization of industrial-sponsored courses, both online and in-person, given by doctors who are renowned in their discipline. ■

Focus

Curie welcomes foreign doctors

Allowing foreign doctors to come and train at Institut Curie is possible within the framework of European programs, such as the EMERALD program, for which a first doctoral student was recruited following a European call for tender. In addition, Lebanese doctors wished to complete their training at Institut Curie, as part of a Fellowship program set up with the logistical support of the Advanced Training Office, for five practitioners and researchers.
As proof of the attractiveness of Institut Curie, 140 doctors applied to do a training course there, even if not all of them were accepted, especially in the context of the pandemic.

United for developing new treatments



2,410
patients included in a clinical study

244
CLINICAL STUDIES
under recruitment
(**12** studies include only minors,
195 studies include only adults,
37 studies include minors and adults)

195
phase I, II and III trials
including **618** patients,
for **1,209** screened' patients

178
minors included in clinical studies
for **182** minors screened

38
clinical studies, Institut Curie promotion

1
Department of Translational Research

4
SiRIC labelled research teams

4
translational research groups

BREAST CANCER – Coordinated by Prof. François-Clément Bidard & Fatima Mechta-Grigoriou
- 31 publications with an impact factor greater than 10 (+ 50% compared to 2020).
- Support for 2 emerging projects for an amount of €60,000 thanks to public generosity. (IMMUNOMAC led by Michel Wassef and FAC-BRCA1 led by Julie Helft).
- 9.9 million euros granted for the CASSIOPEIA project led by Fatima Mechta-Grigoriou "Targeting cancer-associated fibroblasts to combat metastasis and resistance to treatment in triple-negative breast cancer" *(more details on page 7)*.
- 5 national and European funding grants obtained: 4 PLBio (1 Curie lead, 3 in collaboration), 1 WWCR.
- 2 clinical trials accepted in 2021: Serena-6, ALCINA dedicated to T-DXd.

SARCOMES IN ADULTS AND DESMOID TUMOURS – Coordinated by Dr. Sylvie Bonvalot & Josh Waterfall
- Funding obtained for a total of €700,000 to develop the project Deciphering Intertumoral Heterogeneity in Dedifferentiated Liposarcoma.
- A doctoral fellowship obtained for a Doctor of Medicine in the laboratory of Dr. Sarah Watson in the framework of the international PhD program MSCA COFUND - EMERALD Medical Science, co-funded by the European Union's Horizon 2020 research and innovation program.

RADIOTHERAPY AND RADIATION BIOLOGY – Coordinated by Prof. Gilles Créhange & Marie Dutreix
- 62 new publications in 2021.
- 6 clinical trials underway or planned (phase I or II): Neo-Checkray, Nivoglio, Blad-Rad01, Nanorad2, Neopropanc-01, AsiDNA™ Children.
- 2 new patents: a family patent on AsiDNA™, and "A scanning dynamic minibeam collimator" filed by Yolanda Prezado.
- Acquisition of 2 new pieces of equipment: a CT micro-system for small animal imaging, a preclinical imaging micro-system by positron emission tomography (PET) coupled to a HIGH-RESOLUTION CT scanner.

EPIGENETICS – Coordinated by Geneviève Almouzni & Céline Vallot
- Initiation of the spatial-omics working group (3 international meetings in 2021), in collaboration with Labex DEEP and LifeTime.
- Patent filing and publication of the manuscript for the CENPREDICT project (supported by Curie Innov' Booster 2019) for the identification of chromatin biomarker predicting curability of chemoradiotherapy in head and neck cancer.
- Confirmation of support from Curie Innov' Booster 2021 and Emergent/High-Risk project grant 2021, and preparation of a patent (submitted in March 2022) for the IRONSUV project for the discovery and exploitation of a novel iron-dependent targetable domain in a key lysine methyltransferase.

UVEAL MELANOMA – Coordinated by Prof. Nathalie Cassoux & Sergio Roman Roman
- Institut Curie is the world's leading recruiter for the clinical trial of tebentafusp: a bispecific antibody that demonstrates, for the first time, a survival benefit in patients with metastatic uveal melanoma *(see also page 8)*.
- 2 Curie promotion clinical trials have been opened and 5 clinical trials will start in 2022.
- The MBD4 gene mutation is identified as a predisposing factor for uveal melanoma (*JNCI 2021,* Derrien et al.) and as a predictive biomarker for response to immunotherapy (Saint-Ghislain et al, submitted). These discoveries were immediately conveyed into clinical practice: all new patients receive genetic counselling and the MBD4 mutation is now systematically sought.

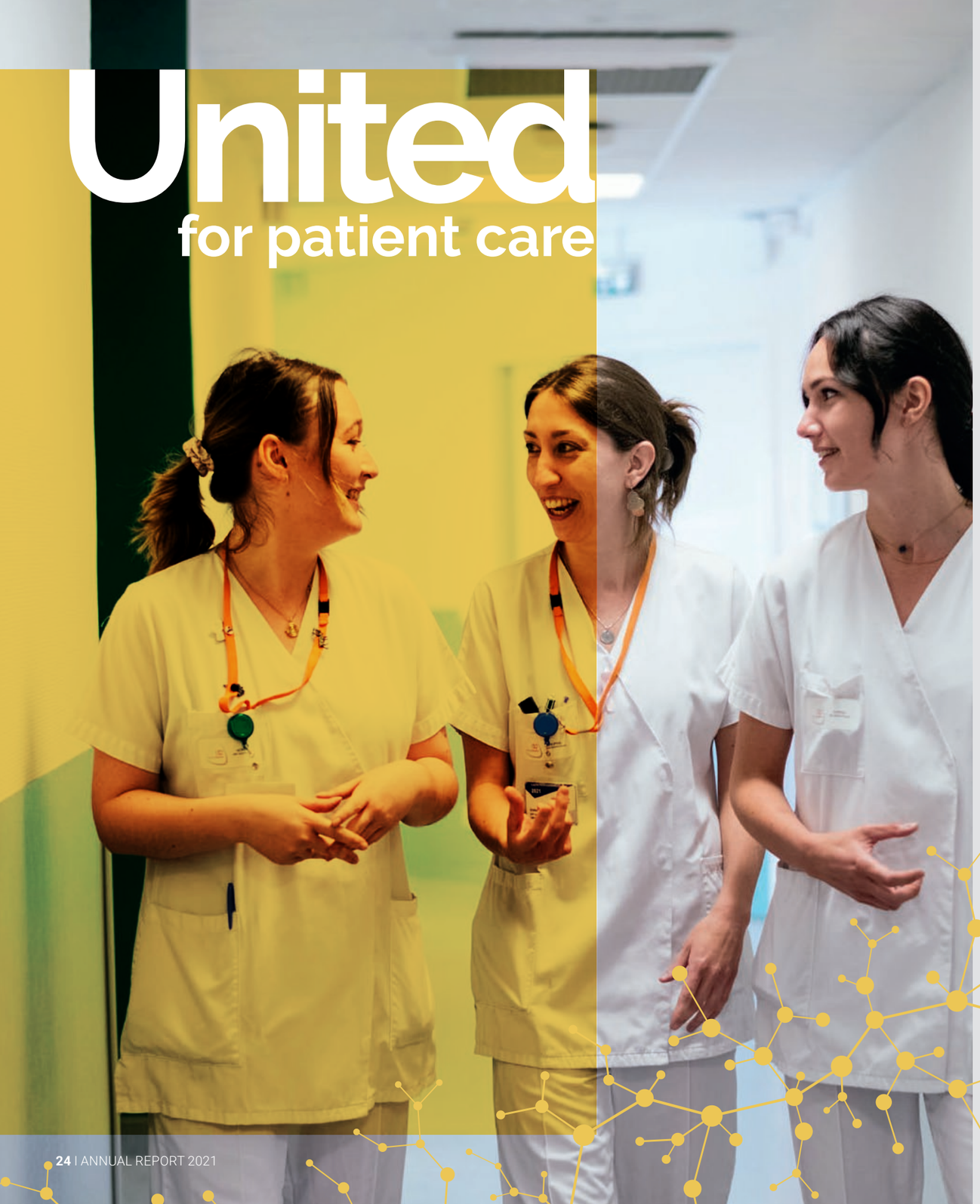
UROLOGICAL CANCER – Coordinated by Prof. Yves Allory & François Radvanyi - New program manager: Daniel Jeffrey (September 2021)
- Identification of a response marker for immunotherapy in advanced bladder cancer (*Eur J Cancer 2021,* Groeneveld et al.).
- Characterisation of intratumoral heterogeneity in basal bladder tumours (*J Pathol 2021,* Sirab et al.).
- Implementation of the THOR/THOR-2 clinical trial (Janssen) in collaboration with the Medical Oncology and Urology teams of the Diaconesses Croix Saint-Simon hospital group: Phase 3 study evaluating erdafitinib in comparison with vinflunine, docetaxel or pembrolizumab in patients with advanced urothelial cancer and pre-selected alterations of the FGFR genes.
- Start of the HOPE clinical trial (NCT05141383): Comparative study of diagnostic and prognostic biomarkers of prostate cancer in liquid biopsy in association with Mondor and IMM (scientific coordination: Antonin Morillon; clinical IP: Prof. Yves Allory).

IMMUNOTHERAPY – Coordinated by Prof. Sebastian Amigorena and Dr. Emanuela Romano
- December 2021 – Obtained UHR funding from the ANR (Agence nationale de la recherche) (10 million euros) for the EpCART project (2022-2027) coordinated by Prof. Sebastian Amigorena and Dr. Marion Alcantara aimed to develop original CAR-T cells designed in academia and to obtain authorization for first injection in humans (IND) from the ANSM in order to launch a phase I/II clinical trial of cell therapy in oncology at Institut Curie (Early trial). This UHR project is a collaboration between the Immunity and Cancer unit (Inserm U932), the start-up Mnemo Therapeutics and the MEARY cell and gene therapy center at the Public Assistance - Paris Hospitals. *(More details on page 7)*.
- More than 10 patents filed in 2021.
- 96 publications in immuno-oncology in 2021.
- The cancer immunotherapy center continues to include patients in some forty clinical trials in various indications: thoracic, ENT, breast, pancreatic, thymoma and uveal melanoma cancers.
- More than 2,000 patients followed by the clinical immunology laboratory co-led by Dr. Olivier Lantz and Cécile Alanio.

THORACIC CANCER – Coordinated by Prof. Nicolas Girard & Dr. Olivier Lantz
- 14 contracts obtained in 2021.
- More than 60 patients have been included.
- CURIMMUNO cohort: 300 patients were treated with immunotherapy alone or with immunotherapy + chemotherapy.
- PRECISION PREDICT cohort: 200 patients were treated with EGFR TKI.

PEDIATRIC AND YOUNG ADULT CANCER – Coordinated by Dr. Olivier Delattre & Prof. François Doz
- Launch of the PREDCAP national database on genetic predisposition to cancer (coordination Franck Bourdeaut).
- Implementation of genetic counselling for all patients of the SIREDO Center.
- International programs Trials: Nant, INFORM2, Alectinib, Avelumab/Lentractinin, AsiDNA™.
- European study MycKids on rare childhood cancers (coordination Dr. Daniel Orbach).
- Immunotherapy project in Ewing's sarcoma supported by the Ligue Nationale Contre le Cancer (coordination Dr. Olivier Delattre).

EARLY TRIALS – Coordinated by Prof. Christophe Le Tourneau & Prof. Aurélien Latouche
- Implementation of the national monthly Cancer of Unknown Primary Origin MCM as part of the France Genomic Medicine 2025 plan.
- Launch of the international real-life clinical genomic database WAYFIND-R.
- Launch of the phase I first-in-human CLEVER PEPTIDE trial from an Institut Curie start-up.
- Obtained SIGNI'T funding from the ARC to identify biomarkers of resistance to immunotherapy in ENT cancers.



METASTATIC BREAST CANCER

PACOSME PROGRAM: A PATIENT SPECIFIC PATHWAY

For 65% of women surveyed by the mental burden study of patients with metastatic breast cancer (carried out by the Collectif 1310[1] in August 2020), receiving the diagnosis of metastatic breast cancer is the most painful stage of their illness. This is why Institut Curie, supported by the Carnot scheme, announced in June 2021 the development of the PACOSME program, a diagnosis delivery and coordination pathway specifically dedicated to these patients. This large-scale project, which started in June 2021, and which will last three years, is led by Dr. Pauline Vaflard and Dr. Paul Cottu and supported by Pfizer. The PACOSME program provides the various healthcare professionals involved with training and coordination in order to offer patients with optimal care and support when the metastatic disease diagnosis is delivered.
In 2021, the first stage of this project was focused on identifying and analyzing patient needs with the support of the Patients Network Association (Patients en réseau). It identified the expectations of the healthcare professionals involved and supported the training of healthcare staff. The year 2022 is dedicated to the structuring and implementation of the PACOSME pathway. Laetitia Lenne (the project's referral nurse) and Silène Delorme (the therapeutic education referral nurse) have organized working groups with the nurses of the Curie day hospital with the aim of starting PACOSME consultations in June 2022.

(1) The 'Collectif 1310' is a group of patient associations that gives a voice to people facing metastatic breast cancer, an advanced and aggressive form of cancer.

QUALITY

The French National Authority for Health's (HAS) certification visit of the Hospital Group is one of the priorities of Institut Curie's medical project. The purpose of this visit is not to evaluate the technical skills of our staff, but to check, notably, that we work as a team within and between departments. It is also to ensure that we consider the results of the various evaluation mechanisms to define improvement actions for the quality and safety of patient care. To strengthen the evaluation process in the field and to enable the deployment of the new HAS audit methods, the structure of the internal auditors' unit has been completely revised. Thus, in 2021, the internal auditors' unit consisted of 77 internal auditors, who conducted 79 internal audits, compared to 10 in 2020 and 16 in 2019. In a very positive cross-functional approach, this improvement process is helping us to correct our areas of concern."

Sophie Oger Hodge,
Quality & Risk Management Director

CIRCULATING BIOMARKERS

EVALUATING THE EFFICACY OF CHEMOTHERAPY: A CLINICAL STUDY UNDERWAY AT INSTITUT CURIE OFFERS HOPE

Today, the performance evaluation of a new chemotherapy is mainly based on radiological examinations and can take months. And yet, monitoring quantitative variations in circulating tumor DNA molecules (tcDNA) in the blood could provide a quick way to determine whether a cancer is responding to chemotherapy. This innovative trial, called MONDRIAN, could radically change the way metastatic disease is managed: reducing the time needed to assess treatment efficacy, avoiding radiation, and giving clinicians a head start by allowing them to offer new chemotherapies before the cancer progresses. tcDNA monitoring would also rule-out chemotherapies that are not effective enough on a given cancer thus reducing prolonged exposure and side effects. This trial, which started in June 2021, includes some 214 patients over three and a half years."

Prof. François-Clément Bidard,
Medical oncologist, principal investigator of the study

TRAINING

Medical administrative offices: an innovative integration program to improve efficiency

The job of a medical administrative assistant in a cancer center such as Institut Curie is very specific. As such, training new recruits is key to making them autonomous and efficient as quickly as possible. The Hospital Group has invested to provide a shadowing program with the medical assistants already in place. For example, two medical administrative assistants, Laurence Aumiot based at the Saint-Cloud site (left) and Cyrielle Laine based at the Paris site (right), specialize in coaching their new colleagues within a dedicated program (specialized teaching path). They welcome new employees and trainees to the medical administrative offices, integrate them and teach them the basics of the job at Institut Curie. In 2021, 53 of the 190 or so medical administrative assistants and secretaries in the Hospital Group completed this program. *"This innovation has been a success, meeting the initial objectives whole heartedly. Thanks to this system, the new recruits feel supported and fully capable of completing their tasks in our beautiful house. After three years of practice, all the teams are unanimous about the essential role played by Cyrielle and Laurence,"* says Valérie Huret, Director of Medical Administrative Officers at the hospital.

PEDIATRICS

European harmonization of very rare childhood tumor management: SIREDO at the forefront

As part of the European PARTNER (Paediatric Rare Tumours Network - European Registry) project, a group of oncopediatricians from 20 different countries, has published harmonized diagnostic and therapeutic recommendations throughout Europe for 8 very rare childhood tumors. This group is led by Dr. Daniel Orbach, Deputy Clinical Director of the SIREDO(1) center at Institut Curie. The end goal of this management harmonization is to be able to evaluate the effectiveness of therapeutic proposals and to ensure that they evolve over time if necessary. The next stage of the PARTNER project consists of collecting clinical data from these young patients on a European scale within a common database to get a better blueprint of these children's future, and to know, in particular, if these recommendations should be modified.

Pediatric Blood and Cancer 2021

(1) Care, Innovation & Research in Childhood, Adolescent and Young-Adult Oncology.

DIGITALISATION

Deployment of digital pathology at the DTMD

The Diagnostic and Theragnostic Medicine Department (DTMD), headed by Dr. Anne Vincent-Salomon, is preparing for its switch to digital technology in the summer of 2022. *"Instead of using a microscope to analyze glass slides containing tissue sections from biopsies, scanners will transform them into digital images,"* explains the manager, who believes that this artificial intelligence tool will make diagnosis almost 100% reliable for the most common cancers as well as for rare cancers, by distinguishing between *in situ* and infiltrating cancers. A project team made up of pathology technicians from the Paris and Saint-Cloud sites and the specialist company Sectra, is supporting the DTMD teams until the project's full deployment, scheduled for September 2022.
These blade scanners have already enabled the DTMD to integrate in industrial partnerships in pathology in 2021, notably with Ibex, an Israeli start-up, as well as research projects between several research units at Institut Curie and Mines Paris - PSL to predict the presence of a DNA repair defect linked to BRCA1 and BRCA2 mutations. Institut Curie also receives samples from partner institutions to sequence tumors or blood to define the cancer predisposition of patients.

In 2021, the DTMD teams really rallied together to collectively choose the slide scanners and the image management system that connects these slides to the patients' medical records."

Dr Anne Vincent-Salomon,
Head of the Diagnostic and Therapeutic Medicine unit (DTMD)

RADIOTHERAPY

Even shorter radiotherapy

The hypo-fractionated radiotherapy approach developed by Institut Curie doctors treating elderly breast cancer patients with no high risk of relapse, consists of reducing the number of sessions to simplify access to treatment. Since 2021, Institut Curie has been one of the first cancer centers to offer selected patients a treatment protocol in just 5 days, with one session per day. This represents a considerable gain in terms of quality of life for patients.

LUNG CANCER

The Precision Predict study opens, Health Data Hub grand prize

Winner of the Health Data Hub's call for projects in 2020, the Precision Predict study, launched in 2021, aims to analyze more than 1,000 lung cancers with EGFR mutations. This project is the result of a collaboration between clinicians and researchers from nine cancer control centers and is led by Institut Curie and coordinated by Professor Nicolas Girard, oncologist, and pulmonologist at the head of the Curie-Montsouris Thorax Institute (inset).
Its aim is to create a clinical and medical imaging database (X-ray and PET scans) of patients with bronchopulmonary cancer with an EGFR-activating mutation and treated with targeted therapy. It will provide a better understanding of response heterogeneity of bronchial cancers to targeted therapies.

ENVIRONMENT

THE OPERATING ROOM GOES GREEN

In the operating room, the consumption of highly-pollutant anesthetic gases has been reduced by a third over five years. That's the equivalent of 73 tons of CO_2 and a saving of 23,000 euros per year since 2016 by the Anesthesia, ICU, and Pain Management department at the Paris site."

Dr. Jane Muret,
head of the Anesthesia, ICU, Pain Management department, Paris site

A system for sorting waste from to the most common surgical acts and recycling plastic parts has been set up in the Saint-Cloud operating room. Since April 2021, 25 kg of waste per month has been recycled, or 300 kg in one year."

Dr. Aline Albi-Feldzer,
head of the Anesthesia, ICU, Pain Management department, Saint-Cloud site

ONCOGENETICS

BREAST AND OVARIAN CANCER SUSCEPTIBILITY GENES: A MAJOR STEP FORWARD IN THE IDENTIFICATION OF BRCA1 AND BRCA2 VARIANTS

Between 5 and 10% of breast cancers are hereditary, i.e., attributable to genetic alterations that very often involve the BRCA1 and BRCA2 genes. These genes are involved in the repair of certain DNA alterations. Being a carrier of an alteration (or pathogenic variant) in one of these genes does not systematically result in the appearance of a cancer, but it does considerably increase the risk of developing one. The variants of these genes are numerous and not all of them are associated with an increase in tumor risk. Their classification as pathogenic or non-pathogenic variants is a major issue. The first results of the COVAR (COsegregation VARiant) study, which was conducted in France for more than 10 years by Institut Curie's genetics department directed by Prof. Dominique Stoppa-Lyonnet (photo opposite), have classified 100 variants of the BRCA1 and BRCA2 genes, using an analysis method that involved the families. These 100 variants involved more than 1,600 families. The aim of this project is to improve diagnostic genetic tests to allow for better adaptive management of patients and their relatives and allow them access to specific anti-tumor treatments such as PARPi.

American Journal of Human Genetics 2021, Caputo et al.

PANCREATIC CANCER

A clinical trial to boost the effectiveness of immunotherapy

Apart from chemotherapy, medical science has not yet found an effective answer to metastatic pancreatic cancer. Immunotherapies do not work well on these types of rapidly progressive cancers because they are poorly recognized by the immune system. A clinical trial promoted by GERCOR (TEDOPAM PRODIGE 63 study) is underway at Institut Curie and led by Dr. Cindy Neuzillet, gastroenterologist, and digestive oncologist responsible for the digestive pathway at the Saint-Cloud site (inset): *"Our aim is to evaluate the effectiveness of an immunotherapy using the anti-tumor vaccine Tedopi (which enables lymphocytes to be 'educated' against proteins produced by the tumor) in association with chemotherapy. This represents real hope for prolonging the survival of patients."*

CANCERS OF UNKNOWN ORIGIN

A multidisciplinary consultation meeting for cancers of unknown origin

Between 2 and 3% of cancer cases, or about 7,000 patients per year, are diagnosed with metastases, without it being possible to determine which organ was first affected. As part of the France Genomic Medicine 2025 plan, two very high throughput genomic sequencing platforms have been created in France, including the SeqOIA platform, which brings together Institut Curie, the Public Assistance - Paris Hospitals and Gustave Roussy. Thus, the contribution of high-throughput sequencing to the treatment of certain patients is gradually becoming a reality. This is the case for patients with cancers of unknown origin, for whom Prof. Christophe Le Tourneau has set up a national MCM (multidisciplinary consultation meeting) with the D3i(1). *"Since the summer of 2021, a national MCM made up of around thirty oncologists, pathologists and molecular biologists has been meeting remotely every month to refine the diagnosis of these patients,"* he says. *"Anatomical pathology testing and additional examinations are requested to improve the diagnosis and try to determine the origin of the cancer. This MCM also seeks to identify molecular alterations that could lead to targeted therapy or immunotherapy."*

(1) Created in 2018, the D3i for the Department of Drug Development & Innovation or the Department of Early Clinical Trials, is a hospital department in which patients are treated with drugs not yet marketed. It is headed by Prof. Christophe. Le Tourneau who manages the MCM (multidisciplinary consultation meeting) at Institut Curie and the link with SeqOIA. Finally, the D3i coordinates research projects related to early clinical trials and precision medicine.

SURGERY

Covid and the resulting HR difficulties have forced the conventional surgery department to review its organization and medical practices. *"Since May 2021, one-third of the department has been closed due to the absence of nursing staff and nurses. Our objective was to maintain the therapeutic excellence to which patients and caregivers are accustomed. This meant, first and foremost, respecting surgery deadlines, which are essential for maintaining a patient's chance of remission intact,"* explains Dr. Olivier Choussy, surgeon and head of the Department of Surgery. We had to reinvent ourselves and rethink our operating methods by transferring part of our conventional surgical activities in gynecological and senological plastic surgery, digestive surgery, ophthalmological surgery, and ENT surgery to ambulatory surgery instead. All the teams have shown admirable investment and solidarity in the implementation of these changes. Some of the new processes have proved to be beneficial in the long term – they facilitate the recovery of patients after their operation - and are now being continued.

Dr. Olivier Choussy,
Surgeon and head of the Department of Surgery

Focus

Adaptability and responsiveness to recruitment difficulties

From the beginning of 2021, Institut Curie has had to face a major and unprecedented challenge: the lack of staff in all departments. To guarantee that care is given safely throughout the health crisis and beyond, the hospital group staff pulled together to provide quality care without sacrificing their efforts and energy.

« In order to overcome these difficulties, in-depth work has been undertaken since September 2021 to find solutions to recruitment problems and to support the remarkable work of all of the teams. This work will continue in 2022 and will include the essential notions of quality of life and working conditions for employees,» adds Anne-Claire de Reboul, deputy director of the Hospital Group and acting director of Human Resources.

«We have continued to treat and welcome our patients within the conditions of well-being and empathy that they deserve. The quality of care provided at Institut Curie is non-negotiable and is very important to us. We have experienced a great deal of solidarity between the different departments of the hospital group, bearing in mind the lack of resources. A situation we have never seen before at Institut Curie. I would like to thank them sincerely for this,» says Sylvie Arnaud, Director of Care.

To improve patient well-being

Valued internationally, supportive care includes a clinical research dimension, as demonstrated by the SHARE project launched in June 2021. Supportive care improves the well-being of patients through the clinical pathways set up at Institut Curie.

Institut Curie is a forerunner in this field, its research activity around supportive care has existed for a long time, but was not really known until now," says Professor Carole Bouleuc, head of the Inter-disciplinary Department of Supportive Care department of the Hospital Group. The creation in June 2021 of the SHARE center (a research center in human and social sciences and outcome research) will make it possible to structure and group together all the research activities relating to patient quality of life, palliative care, onco-geriatrics, nutrition, and patient empowerment. SHARE is led by Anne Bredart and Dr. Sylvie Dolbeault, researchers in psycho-oncology, authors of a large number of international publications and leaders of humanities and social science research projects within the various SiRIC programs (SIte de Recherche Intégrée contre le Cancer or Integrated Cancer Research Institute).

Physical activity and sexuality of patients under care

"Since its launch, the adapted physical activity platform (APA) has included more and more patients," says Professor Carole Bouleuc. A three-stage care pathway has been set up, and includes raising awareness sessions during patient conferences, the prescription by the oncologist of an adapted physical activity mentioning any limitations or precautions, and then the inclusion of patients in STARTER programs with Institut Curie's sports partners either in the hospital or remotely.

Finally, a study was carried out in 2021 to set up a care pathway in onco-sexology, enabling patients' sexuality problems to be dealt with. A multidisciplinary working group involving oncologists, radiotherapists, psycho-oncologists, and nurses has defined a clinical pathway which will be available to patients in September 2022. ■

New imaging equipment for Institut Curie

The acquisition or renewal of functional or interventional imaging equipment enables better patient care by improving the quality of examinations. They complete the arsenal of techniques already available at Institut Curie.

A major upgrade of one of the Paris site's MRIs was carried out (change of the radiofrequency chain without changing the magnet). Radiologists now have better quality and faster sequences for patients and access to more efficient functional imaging techniques, such as perfusion and diffusion imaging. Similarly, SPECT-CT equipment (X-ray scanner with gamma camera) was replaced by a state-of-the-art device which has improved image quality while optimizing the dose delivered to patients.

In 2021, a cooperation protocol was set up between the Paris site and the Paris-Nord Est hospital group (Aulnay-sous-Bois, Montreuil and Montfermeil) for the care of patients with gynecological and breast cancer. A radiologist has been hired on a part-time basis in both establishments. Every fortnight, surgeons, medical oncologists, radiologists, and radiotherapists meet by videoconference to establish the right indications and define the best treatments for the patients.

Interventional radiology on the rise

Interventional radiology (IR) refers to procedures performed percutaneously with radiological guidance. Diagnostic IR corresponds to deep biopsies that collect tumor samples to characterize tumors and search for therapeutic targets. Its use is growing considerably in the activity of radiologists. Therapeutic IR replaces or complements conventional oncology treatments through various imaging-guided techniques (ablathermy radio frequency or cryotherapy, cementoplasty, neurolysis, etc.). In 2021, Institut Curie acquired mobile cryotherapy equipment; the indications for this technique are developing for the treatment of metastases, particularly in certain desmoid tumors, but also probably for certain primary tumors in the future. ■

"The activity of diagnostic interventional radiology is growing steadily and now represents a very important part of the activity of radiologists. This activity has now reached very high levels and is very important for research, whether it involves the detection of therapeutic targets or more fundamental research on adult and child cancers."

Dr. Hervé Brisse,
Head of the Medical Imaging department

3,000
BREAST BIOPSY PROCEDURES
per year over both sites

2,000
DIAGNOSTIC BIOPSIS
not including senology

United in the fight against cancer

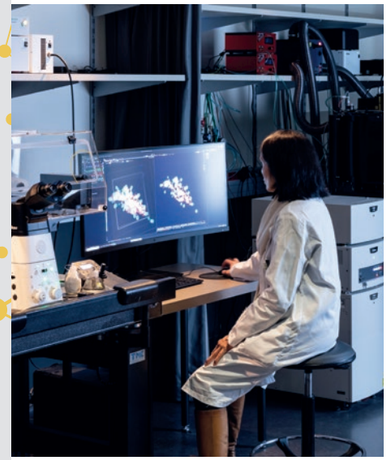
Outstanding results in innovation and industrial partnerships

After a decade of growth, Institut Curie intends to accelerate the transfer of research results to companies. Its objective? To develop ever more therapeutic innovations for the benefit of cancer patients.

Since 2016, Institut Curie has had an ambitious policy for the detection and the fruition of discoveries, favoring research partnerships with industry and providing greater incentives for the creation of start-ups. This innovation acceleration strategy is supported by the Technology Transfer Office (TTO), which is genuinely involved in all stages of technology transfer. Everything is done to identify at a very early stage the scientific projects at the origin of future therapeutic innovations and technologies that could be developed by Institut Curie.

A virtuous circle for innovation

Innovation grows from fertile soil thanks to the excellence and creativity of Institut Curie's fundamental, translational, and clinical research, which is capitalized on by the teams of the Technology Transfer Office. To make researchers aware that innovation can come from their daily practices, an internal network of tech transfer ambassadors (TTA) has been set up. This group now has 19 members from a wide variety of units in the Research Center and departments within the Hospital Group. Among them are project leaders, LabEx managers and volunteer engineers, who will be trained and informed, and are now the Technology Transfer Office's intermediaries on the ground. Close to their teams, they disseminate key information to them on transfer procedures and opportunities for tender development, and report on projects in progress in the laboratories, thus facilitating their analysis and early monitoring by the Technology Transfer Office. Intellectual property expertise at Institut Curie, a key element in



"In addition to its recognized successes in transferring technologies from Institut Curie to the economic world, the TTO also focuses on the downstream part of this process. Our ambition is to strengthen the detection and support for project fruition. Thanks to the deployment of this network of tech transfer ambassadors, we are in daily contact with innovation stakeholders at Institut Curie's sites. This is one of the reasons for the success of our strategy. The number of patents granted each year is also a demonstration of our efficiency. It is worth noting that 70% of our over 30-month-old patent portfolio has been transferred to an industry."

Cécile Campagne,
Director of Technology Transfer Office
Deputy Director of Carnot Curie Cancer

56
PATENTS ISSUED

200
PATENT FAMILIES, which represent more than **800 titles** in Institut Curie's portfolio

60
invention claims

19
tech transfer ambassadors

■■■ accelerating innovation, has also been strengthened by the "French patent attorney" certification obtained by the head of the Intellectual Property Unit at the end of 2021. This is a first in six years for Institut Curie. The recognition of this expertise testifies to the professionalization of the tech transfer professions within Institut Curie.

Carnot provides essential support

Institut Curie was awarded the Carnot Curie Cancer label in 2011, which has since been renewed twice, and is part of this network of excellence that supports academic research institutes in developing company partnership searches. Obtaining this label and the associated funding has helped generate new projects and raise the professional level of the development team. One example is Institut Curie's internal development program Curie Innov', whose budget has been increased thanks to Carnot funding, allowing support for five innovative projects in 2021.

Some seven start-ups from Institut Curie's incubation program are more advanced in their development and they have been able to raise more than €140 million from investors. Among them, two spin-offs achieved record top league results in the two years following their creation: Egle Therapeutics (from the work of Eliane Piaggio's team), which raised €40 million for the development of first-in-class immunotherapies, and Mnemo Therapeutics (from the work of Prof. Sebastian Amigorena's laboratory), a biotech company dedicated to advanced CAR-T therapies, which achieved a record for a European start-up by raising €75 million. These exceptional amounts demonstrate the effectiveness of this original and integrated program as well as the interest of investors in innovations with high therapeutic potential emerging from Institut Curie. Ribonexus, a start-up created thanks to the combined scientific and medical expertise of its co-founders (Stephan Vagner, unit director at Institut Curie, and Prof. Caroline Robert, head of the Gustave Roussy Dermatology department), which develops new-generation treatments capable of overcoming resistance to targeted tumor cell therapies, has benefited from this exceptional dynamic around Institut Curie spin-offs by raising €4 million since it started. ■

140.6
million € raised for Institut Curie start-ups

At least
224
jobs created between 2002 and 2021 in the 28 start-ups that have emerged from Curie's incubation program

50
NEW PRODUCTS OR SERVICES
put on the market since 2002

Focus

Two in-house start-ups return to Institut Curie

Discovery, maturation, development, fundraising, drug candidate development etc., the road to the patient's hospital bedside remains long. Once all these stages have been completed, some start-ups bring their project to fruition by carrying out their clinical trials within Institut Curie's Hospital Group. PEP-Therapy, a biotechnology company specializing in the development of penetrating peptides as targeted therapies for the treatment of cancers, has obtained authorization from the French National Agency for the Safety of Medicines (ANSM) to conduct clinical trials of its drug candidate, PEP-010.
For its part, Onxeo entered into a research agreement to conduct a phase 1B/2 trial evaluating ASIDNA™ in combination with radiotherapy in the treatment of recurrent high-grade glioma in children. Finally, Institut Curie was the first hospital in the world to acquire AVATAR MEDICAL's virtual reality technology which facilitates surgical procedure and originated from research conducted at Institut Curie by the team of the late Maxime Dahan and Mohamed El Beheiry and Jean-Baptiste Masson's team at Institut Pasteur.

Working with a start-up «made in Curie» is in our DNA! D3i was created in 2018 to formalize everything we were doing in terms of innovation in the Hospital Group, in conjunction with the Research Center. As the sponsor of the PEP-Therapy clinical trials at Institut Curie, we wrote the protocol and included the patients. Institut Curie offers an extraordinary environment for drug developers, as we are able to set up projects from start to finish."

Prof. Christophe Le Tourneau,
Head of the Department of Drug Development and Innovation (D3i)

PEP-Therapy is developing PEP-010, an innovative peptide used as a targeted therapy for the treatment of cancers, resulting from research conducted at Institut Curie. It seemed obvious to us to continue to collaborate with Institut Curie, a center of world-renowned excellence, to conduct our pre-clinical studies in relevant animal models. Institut Curie is now the main center where the Phase Ia/b clinical trial of PEP-010 is being conducted."

Antoine Prestat,
CEO of PEP-Therapy

Institut Curie continues its international commitment

All over the world, Institut Curie contributes to the fight against cancer. It welcomes patients and carers from all continents and carries out training and support activities abroad to develop the care solutions for cancer care.

"Confronted with the global challenge of cancer, the number of cases of which could, according to the WHO, increase by 60% in the next 20 years, Institut Curie is forging partnerships with hospitals, carers, and doctors throughout the world in order to share its know-how, expertise and knowledge," explains Dr. Pierre Anhoury, Director of International Relations. Projects are multiplying on all continents, from Japan to Kazakhstan, via Colombia, Kuwait, Lebanon, Jordan, and Tanzania, where, since the end of 2019, Institut Curie has been a consultant for the French Development Agency (FDA). The Tanzania Comprehensive Cancer Project provides for the construction of care facilities, the training of health workers specialized in cancer and the purchase of radiotherapy equipment.

Despite the health crisis, Institut Curie has remained true to its tradition of welcoming patients from all over the world for cancer treatment. In 2021, 286 patients with complex or rare forms of cancer or who had problems accessing care in their own country were able to benefit from these services. Their chances of recovery have been improved by this care in France, within the institute.

In addition to its healthcare activities, Institut Curie's international reputation is also reflected in the excellence of its scientific research. Institut Curie's research center attracts many young researchers from all over the world to its laboratories. 74 nationalities were represented in 2021. Some 68% of post-docs and 42% of PhD students were foreign. ■

286
FOREIGN PATIENTS
received in 2021

15
master classes and courses given abroad in 2021

300
PARTICIPANTS
attended an Institut Curie course abroad

Donors, always on hand

In 2021, despite the health crisis, Institut Curie's donors have been present and loyal. Their generosity is at the heart of the Hospital Group and the Research Center's operations. By supporting scientific and medical innovation, they help to develop research and improve patient care. Thanks to these donors, many projects have been supported in the fields of care, research, and the transmission of knowledge. Here is a look at two of them.

Care: adapted physical activity accessible to all

Adapted physical activity is now considered a non-drug treatment for cancer. It helps patients to cope better with treatments and to limit relapses. Some patients, because they live far from a sports center or have time constraints, cannot participate in these on-site workshops. This was especially the case during the Covid crisis. In 2021, the gifts received made it possible to develop remote adapted physical activity workshops, via a smartphone application in partnership with KIPLIN, a digital application publisher specializing in the health sector. This is a major step forward in enabling all patients to access the benefits of physical activity.

Research: state-of-the-art equipment for translational research

Researchers from the Translational Imaging in Oncology laboratory (Inserm U1288), headed by Irène Buvat, Director of Research at Institut Curie, have acquired a preclinical PET (Positron Emission Tomography) scanner. This acquisition is a major step towards validating new radiopharmaceutical compounds targeting the functions of molecules associated with cancer and thus obtaining precise images to better understand them. ■

242,000
DONORS

31.1
million € of gifts and sponsorship in 2021

26.7
million € of bequests in 2021

Large scale fundraising

A DAFFODIL AGAINST CANCER

The 17th edition of the national campaign "*Une Jonquille Contre le Cancer* (Great Daffodil Cancer Appeal)", which ran from 9 to 21 March 2021, adapted to the health crisis and had to reinvent itself with an entirely digital edition. In 2021, the campaign particularly wanted to highlight the importance of artificial intelligence and big data to accelerate research and innovation in cancerology. Thanks to everyone's dedication: volunteers, partners, sponsors, associations and local authorities, this fundraising campaign exceeded the initial target of 700,000 euros, reaching a record 892,000 euros in gifts.

RACE OF LIGHTS: LIGHT UP THE NIGHT SKY AGAINST CANCER

5,000 runners and walkers came together in name of solidarity on Saturday 20 November 2021 in the heart of Paris to light up the night sky against cancer. After a 2020 edition only in connected mode, due to the pandemic, the light bearers were happy to meet up again at the Place de l'Hôtel de Ville in Paris. They walked or ran along the banks of the Seine in a united team spirit. Some 100 companies had also formed teams of sports men and women. This tremendous coming together raised €130,000 in gifts to support research for the benefit of all patients.

3rd edition of the Open Golf Tournament

For its 3rd edition, Institut Curie Golf Open at the Golf de Joyenval (78) took place on 24 October 2021, under the patronage of actor Roschdy Zem. This competition attracted some 72 participants from 9 companies in support of the fight against breast cancer.
The 113,000 euros raised went to support the TEP-FES project of Dr. Audrey Bellesoeur and Dr. Romain-David Seban. The aim? To develop a new imaging technique that limits the need for biopsies in the treatment of women with metastatic breast cancer.

Mobilized partners

Gamers take action against pediatric cancer

Live from Rennes, hundreds of fans of the video game "The Legend of Zelda" took part from 9 to 11 July 2021 in a live marathon broadcast on the Twitch streaming platform. The principle of this virtual event was to play for 48 hours non-stop in order to raise public awareness and encourage viewers to support research against childhood cancer at Institut Curie. 15,000 € were collected thanks to this first mobilization of young gamers.

The Solitaire du Figaro sailing race with Mutuelle Bleue

Institut Curie participated for the first time in the Solitaire du Figaro, thanks to its historical sponsor Mutuelle Bleue. At the helm of "Mutuelle Bleue pour l'Institut Curie", an orange and blue Beneteau 3 sailboat, skipper Corentin Horeau set off from Saint-Nazaire on 22 August 2021 for the 52nd edition of the race, finishing one month later in 8th place. The aim of this partnership was to raise public awareness of the 40% of cancers that can be prevented - a real public health issue.

The Hubert Gouin - Childhood and Cancer Association was created 18 years ago, when my son Hubert died of neuroblastoma. By building a discreet network of eminent personalities from the scientific and medical world, we have organized numerous events and have been able to raise 3 million euros for research into pediatric oncology. As a member of the GRAVIR collective, we have been long-time partners of Institut Curie. The medical and nursing teams of its SIREDO(1) center are dedicated to the care of children and young adults suffering from cancer and accompany the young patients and their families with professionalism and empathy during these very difficult times. The association is very involved in the financing of the MICCHADO trial, whose objective is to better understand and characterize resistance to treatment of certain cancers in children. This is a real hope for young patients with 'high risk' cancers."

Anne Gouin,
President of the Hubert Gouin - Enfance et Cancer association (Childhood and Cancer association)

(1) SIREDO (Care, Innovation & Research in Childhood, Adolescent and Young-Adult Oncology) is an integrated care and a research center created by Institut Curie to optimize the care of children, adolescents, and young adults.

100 years: the Musée Curie at the heart of a double anniversary

Through its publications, its cultural program, and the various events it hosts in its rooms or broadcasts online, the Musée Curie (Curie Museum) contributes to perpetuating the scientific heritage of the Curie family. As such, 2021 was a year rich in celebrations.

100 years of the Fondation Curie

For this anniversary, the Musée Curie produced an entire book "1921-2021, de la Fondation à l'Institut Curie" (1921-2021 from its foundation to Institut Curie) dedicated to the history of the institution and distributed to staff and institutional partners. This book was then turned into an exhibition of 14 panels, presented at the three Institut Curie sites and redesigned in an itinerant version for the United States. The museum also hosted the filming of the documentary "Fondation Curie: 100 years of generosity against cancer", which was broadcast exclusively to all staff on 21 May, the anniversary date, before being made available on curie.fr and the institute's social networks.

The celebration of the 100th anniversary of Marie Curie's trip to the United States resulted in the production of a four-episode web series "Marie Curie, the journey of a lifetime", broadcast on the museum's YouTube channel, as well as one of the five «Rendez-vous au Musée Curie» video clips produced in 2021, dedicated to this American journey.

Finally, the launch of IN2P3's 50th anniversary celebrations[1] was organized live from the Musée Curie on 14 April, in the presence of Antoine Petit, President and CEO of CNRS, and Reynald Pain, Director of IN2P3.

Discovering the museum and explaining radioactivity

Throughout the period of closure imposed on cultural establishments due to the health crisis, the museum team reoriented its activities towards digital productions to enable people to discover the museum from a distance: a dozen videos were put online as well as a recording of the storytelling show «Marie Curie, radium magician», offered as a private streaming show to schools. In addition, the museum took part in several radio broadcasts to publicize the museum, its collections, and the history of radioactivity.

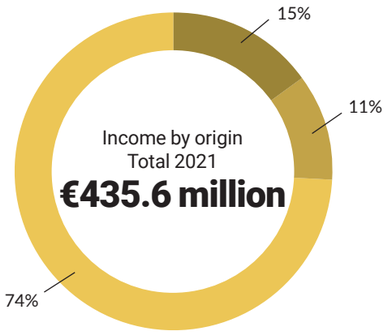
In addition to this mission of transmission, the Musée Curie is also responsible for the conservation of the heritage linked to this scientific adventure. Its action is part of a wider reflection on the need to pass on this memory and all the equipment used at the time, while taking into account the radioactive aspects and the evolution of the regulations. For example, a radium «emanator» was identified in a private home. Once it had been decontaminated, an operation carried out in partnership with ANDRA[2], it was able to join the collections. Finally, some documents were acquired by the Musée Curie, including three letters from Pierre Curie, as well as photographs and old registers. ■

> Our mission is to protect our heritage and pass it on to future generations: we seek to preserve historical radioactive objects, while respecting the basic rules of radiation protection."
>
> Renaud Huynh,
> Director of the Musée Curie (Curie Museum)

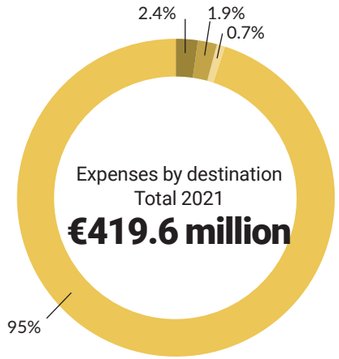
(1) The National Institute of Nuclear and Particle Physics (IN23P) is one of the largest CNRS institutes, to which the Musée Curie is attached as a support and research unit.
(2) French National Agency for Radioactive Waste Management.

Our business model

Public grants play an important role in Institut Curie's total funding, but private funds from public generosity, sponsorship, or the proceeds from the exploitation of its discoveries ensure its independence and are a driving force for innovation in the fight against cancer.



- Grants and other public funding (€323.9 million)
- Income from public generosity (€62.9 million)
- Income not related to public generosity (€48.8 million)



- Social missions (€398.4 million)
- Public generosity fundraising expenses (€10.3 million)
- Operating expenses (€7.9 million)
- Expenses arising from the search for additional funding (€3 million)

Source: information provided by the Income statement by source and destination (excluding items calculated such as changes in provisions, depreciations and dedicated funds).

Hospital Group resources

- Health insurance as a private health establishment of collective interest (Espic) via activity-based pricing (T2A), the contribution to missions of general interest and aid for contractualization (Migac).
- Invoicing of care to non-insured patients (particularly patients from outside the European Union), co-payments and fixed daily rates (with no remaining costs for insured patients).
- Industrialists, sponsors, charities and public or semi-public organizations for clinical research and innovation.
- Generosity of the public (gifts and bequests).

Research Center resources

- Research organizations (CNRS, Inserm, universities): part of the personnel, operating or investment costs.
- Annual grant from the Ministry of Higher Education, Research, and Innovation.
- Public or semi-public funding in response to calls for tender: Agence nationale de la recherche (ANR), Institut national du cancer (INCa), Conseil régional d'Île-de-France, European Research Council (ERC) and European Commission.
- Private funding: patrons, charities (Ligue contre le cancer, Fondation ARC pour la recherche sur le cancer, Fondation pour la Recherche Médicale, etc.).
- Industrialists within the framework of licenses, collaborations, or partnerships.
- Public generosity (gifts and bequests).

Head Office resources

- Financial income linked to Institut Curie's cash flow. By maintaining a certain cash flow threshold, Institut Curie can finance its support and administrative functions by limiting its recourse to public generosity.
- Public generosity and CNRS finance the Musée Curie, the foundation's social mission.
- Proceeds from valorization.
- Income from international consultancy activities.

Asset management

INTANGIBLE ASSETS

Institut Curie holds a portfolio of trademarks and patents. The latter protects inventions resulting from research carried out within the Foundation. These assets are not capitalized in the balance sheet. The exploitation rights attached to the patents are granted to third parties (industrialists, biotechnology companies) through the granting of exploitation licenses.

REAL ESTATE ASSETS

Institut Curie owns some of the buildings on the three sites in Paris (75), Orsay (91) and Saint-Cloud (92) where its social missions are carried out. Additional premises are leased to accommodate tertiary activities. Institut Curie does not own any investment property.

OTHER FIXED ASSETS

In most cases, Institut Curie owns the assets required for its activities, including heavy healthcare equipment and research apparatus. Exceptions include four items of radiotherapy equipment and two items of imaging equipment which were leased.

FINANCIAL ASSETS

Composed of a portfolio of investment securities, these financial assets aim to ensure the long-term viability of Institut Curie's activities, while providing annual resources to ensure its general interest missions.
Their management is governed by a reference framework that was updated following the implementation of Institut Curie's new statutes in 2018. In compliance with the basic principles of prudence, a wide diversification of the type of products and investment supports is systematically sought.
The securities portfolio is managed by the Executive Board, which has set up a Finance Committee to monitor investments and make recommendations.
The management of medium and long-term assets is delegated to service providers which are selected following consultations.
Cash management remains in-house.
The recently initiated policy of socially responsible investment is continuing, as is the diversification into real estate through the acquisition of shares in real estate investment trusts (REITs).
The annual financial management report, as well as the management rules and investment strategy, with an indication of the associated risks, are submitted annually to the Supervisory Board for approval.

Institut Curie at a glance

The governance of Institut Curie is based on a Supervisory Board, a Scientific Council, a Board of Directors and three entities: the Hospital Group, the Research Center, and Head Office.

The Supervisory Board
The main task of the Supervisory Board of is to supervise the management bodies and to ensure the proper management of the Executive Board. It is assisted by 3 *ad hoc* committees.

The Scientific Advisory Board
is composed of international experts - particularly in the field of cancer research - from outside of Institut Curie. It provides strategic advice on the institute's major orientations and activity programs.

The Executive Board
is responsible for the administration and management of Institut Curie in conjunction with the directors of the Hospital Group, the Research Center, and the Head Office. It is vested with the broadest powers to act in all circumstances on behalf of the foundation.

The entity directors
are appointed by the Executive Board after approval by the Supervisory Board. The three entity directors define the strategy of their entity, which they propose to the Executive Board. They are responsible for managing human resources and authorizing expenditure corresponding to the part of the institut budget relating to their area.

The Supervisory Board

Three founding members with voting rights
- **Prof. Stewart Cole,** representing Institut Pasteur
- **Marc Joliot,** representing the Curie family
- **Daniel Thierry,** representing the Rothschild family, Chairman of the Supervisory Board

Six *ex-officio* members with voting rights
- **Jocelyne Bérille,** representing the French Ministry of Higher Education, Research, and Innovation
- **Prof. Gilles Bloch,** representing the French National Institute for Health and Medical Research (Inserm)
- **Jean-Guy de Chalvron,** representing the French Ministry of the Interior
- **Dominique Joseph,** representing the French Economic, Social and Environmental Council (CESE)
- **Prof. Norbert Ifrah,** representing the French National Cancer Institute (INCa)
- **Yvan de Launoit,** representing the French National Center for Scientific Research (CNRS)

Five qualified persons with voting rights
- **Frédéric Donnedieu de Vabres**
- **Prof. Jean-François Girard,** Vice-Chairman of the Supervisory Board and Chairman of the Remuneration Committee
- **Mireille Guigaz**
- **André Gauron**
- **Philippe Louis-Dreyfus**

Four staff representatives with voting rights
College of staff representatives
- **Sébastien Goud**
- **Valérie Sire-Trotin**

Representatives of the scientific and medical staff
- **Prof. Nathalie Cassoux** for the Hospital Group
- **Fatima Mechta-Grigoriou** for the Research Center

Six other members sit in an advisory capacity
- **Alain Fuchs,** representing the PSL University
- **Samuel Guibal,** representing the Paris Local Education Authority
- **Prof. Xavier Jeunemaitre,** Dean of Paris University
- **Marie-Christine Lemardeley,** representing the City of Paris
- **Jean-Christophe Pierson,** representing the City of Saint-Cloud
- **Gérard Wormser**

The Scientific Advisory Board

- **Prof. Edith Heard**
Chairman of the Scientific Advisory Board
EUROPEAN MOLECULAR BIOLOGY LABORATORY (EMBL), HEIDELBERG, GERMANY
Director General

- **Prof. Iain Mattaj**
Chairman of the Scientific Advisory Board (until July 2021)
Director of Human Technopole – Milan (Italy)

- **Anton Berns**
THE NETHERLANDS CANCER INSTITUTE, AMSTERDAM, NETHERLANDS
Director of Research and Chairman of the Board of Directors

- **Prof. Robert G. Bristow**
MANCHESTER CANCER RESEARCH CENTRE (MCRC), MANCHESTER, UNITED KINGDOM
Director
Co-Director, CRUK Manchester Institute
Senior Group Leader, Translational Oncogenomics, CRUK Manchester Institute
Chief Academic Officer & Honorary Consultant, The Christie NHS Foundation Trust
Cancer Domain Lead and University Professor of Cancer Studies, The University of Manchester

- **Prof. Pascale Cossart**
INSTITUT PASTEUR, PARIS, FRANCE
Head of "Bacteria-Cell Interactions" unit (INSERM U604/INRA USC2020)

- **Prof. Alain Fischer**
HOPITAL UNIVERSITAIRE NECKER ENFANTS MALADES, PARIS, FRANCE
Professor at the Claude Bernard Chair of Collège de France (Experimental Medicine)
Director of the Institut Imagine

- **Eileen Furlong**
EUROPEAN MOLECULAR BIOLOGY LABORATORY (EMBL), HEIDELBERG, GERMANY
Head of the Genome Biology department & Senior Scientist

- **Dr. Luca Gianni**
FONDAZIONE MICHELANGELO, MILAN, ITALY
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Chevalier des Palmes académiques 2021
Nuclear Dynamics unit (CNRS UMR3664 / Sorbonne University)

Chloé-Agathe Azencott
First prize winner of Young AI Woman Engineer organized by Tilder in partnership with France Digital and Challenges
Cancer and Genome unit: Bioinformatics, Biostatistics and Epidemiology of Complex Systems unit (Inserm U900 / Mines Paris Tech)

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Carole Bouleuc
Appointed Associate Professor in Palliative Medicine at the University of Paris
Interdisciplinary Department of Supportive Care in Oncology

Déborah Bourc'his
Grand Prix de la Fondation pour la Recherche Médicale 2021
Genetics and Developmental Biology unit (CNRS UMR 3215 / Inserm U934 / Sorbonne University)

Irène Buvat
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Ruban Rose Avenir prize
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Cell Biology and Cancer unit (CNRS UMR144/Sorbonne University)

Ana-Maria Lennon-Duménil
Grand Prix Charles Defforey – Institut de France
Immunity and Cancer unit (Inserm U932)

Sophie Loeillet
CNRS Crystal Medal
Dynamics of Genetic Information: Fundamental Bases and Cancer unit (CNRS UMR 3244 / Sorbonne University)

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Allianz foundation – Institut de France award
Immunity and Cancer unit (Inserm U932)

Mathilde Mathieu
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Immunity and Cancer unit (Inserm U932)

Fatima Mechta-Grigoriou
Raymond Rosen Prize - Fondation pour la recherche médicale 2021
Cancer, Heterogeneity, Instability and Plasticity unit (Inserm U830)

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3rd prize for Oral Presentation from the SFAR meeting (French Society of Anesthesia & Intensive Care Medecine)
Anesthesia and ICU-Pain Department

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Hospital Information System Awards

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Judith Pineau
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Prize for the second inclusion center competing in the Data Challenge 2020

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Dynamics of Genetic Information: Fundamental Bases and Cancer unit (CNRS UMR 3244 / Sorbonne University)

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