ACTIVITY REPORT

TOULOUSE UNIVERSITY CANCER INSTITUTE-ONCOPOLE

—

2020

INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
Oncopole

The Oncopole, as patients and the general public call it, groups together on a single site more than 2,000 professionals engaged in the fight against Cancer, divided between the Toulouse University Cancer Institute-Oncopole (IUCT-O) and the Cancer Research Center of Toulouse (CRCT). The IUCT-Oncopole brings together the expertise and excellence of the Institut Claudius Regaud (cancer care and research center) and several of the Toulouse University Hospital's oncology departments. Its missions are providing the highest standards of cancer care, research and teaching.

The strength of this model, a pioneer in France, lies in pooling the skills of the care and research teams who work together on a daily basis so patients can benefit from a comprehensive care offer at the cutting edge of innovation.

Most of the basic and translational research teams are guided by dual expertise, medical and scientific, a powerful driver of innovation for the treatment-research continuum.

Since its opening in 2014, unprecedented research projects have been recognized and published in prestigious scientific journals, patient care has begun its revolution to meet the new challenges of cancer care, while recent discoveries are now opening up new therapeutic perspectives to prevent and cure cancers in an ever-more personalized way.

The year 2020 has highlighted many of these achievements that we are pleased to share with you in this Activity report.

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International recognition for the Oncopole's excellence

In July 2020, the IUCT-Oncople and the Cancer Research Center of Toulouse (CRCT) were jointly awarded certification as a Comprehensive Cancer Center (CCC) by the Organisation of European Cancer Institutes (OECI).

This honor, the highest level of excellence awarded by this European structure, pays tribute to the strong integration of research into patient care and the quality of the global approach to treatment.
The Oncopole — bringing together the IUCT-Oncople and the CRCT— is thus certified for the next five years. This international recognition places it among the top European centers of expertise in oncology.

"This distinction validates the concept of the Oncopole bringing together on a single site clinicians and researchers to work towards the goal of accelerating the development of new therapies and having access to them, all the while providing the highest quality of healthcare and teaching".
Prof. Jean-Pierre Delord, Administrator of GCS IUCT-Oncopole.

"This certification provides strong European visibility and offers us the opportunity to develop new international collaboration".
Prof. Gilles Favre, Director of the CRCT.

"The Oncopole site won accreditation from the OECI. We are now in the midst of certifying our network, the first of its kind in the world."
Marc Penaud, President of the IUCT-Oncopole General Assembly.

Obtaining this certification marks a first decisive step in making Toulouse a major player in cancerology and a city internationally recognized in the fight against cancer.

The strong points of the Oncopole identified by the OECI experts are:

1. Its strategic vision for the next five years
2. High-level translational research enabling close and fruitful connections between the CRCT and clinical practice
3. The leadership and the exemplary integration of research in radiotherapy
4. The high quality of interactions between clinicians and the pharmacy, the robust organization of pharmaceutical clinical trials
5. The offer of supportive care: its structure, its leadership and its unique organization in Europe
6. The efficacy and quality of the BioBank, its link to research
7. The high level of patient satisfaction

KEY FIGURES 2020

2,036 staff
Of whom **160** physicians
185 interns
165 researchers

11,113 new patients (active hospitalization file)
35,188 patients treated

105,237 hospital stays
Mean length of stay for full hospitalization: **6.07 days**
80.7 % outpatients in hospital departments
306 beds - **94** day-hospital beds
54,754 radiotherapy sessions
224 transplants and **17** patients treated with CAR-T cells

11 technical support centers
217 clinical studies included patients in 2020

13.7 % of patients (active file) included in a clinical trial

782 publications

14 new patents

less than 6 months for a CRCT discovery to be translated into a clinical trial at the IUCT-O

100 solidarity initiatives during the lockdowns
4,430 donors
1 foundation

Prof. Thierry Philip.

A label of excellence for the Oncopole

Professor Thierry Philip, President of the Institut Curie, also chairs the Organisation of European Cancer Institutes (OECI). In 2020, the OECI awarded the Oncopole "Comprehensive Cancer Center" accreditation.

What does this distinction represent?

It is a European certification of excellence —a true international recognition that underlines the quality and medical and scientific skills of the Oncopole— awarded by peers and an independent organization whose method is itself accredited by the International Society for Quality in Health Care (ISQua).

The quality of research, the quality of care, the quality of the organizations, etc., are all evaluated. Thanks to this certification, the Oncopole has become the 23rd "Comprehensive Cancer Center" among 95 European members of the OECI.

What are the strengths that have enabled the Oncopole to obtain this label?

The site's overall strategy and the link between the public and private sectors, with no overlap, was singled out for praise. As well as the quality of the premises, appreciated by the patients interviewed, the extremely impressive growth of the Toulouse Cancer Research Center (CRCT) and the significantly increasing number of publications.

The quality of the laboratories and research units and the balance between young and more experienced researchers.

The significance of radiotherapy was also underlined, thanks to a strongly research-oriented department, linked to high-level projects.

What are the advantages for the Oncopole of being part of a European network such as the OECI?

This recognition and its membership in the OECI will enable the Oncopole to develop its international network. It will be in contact with the best European centers, to engage in collaborations and help centers in Southern and Eastern Europe to develop. The Oncopole teams will also have the opportunity, through the OECI working groups, to bring in and to import the best of each other's work.

What are the OECI's priorities at European level over the next few years?

The OECI is the world's largest network of accredited cancer centers committed to a quality approach. The objective is to be part of the two major European projects underway: the cancer mission and the European cancer plan, in conjunction with the French ten-year strategy.

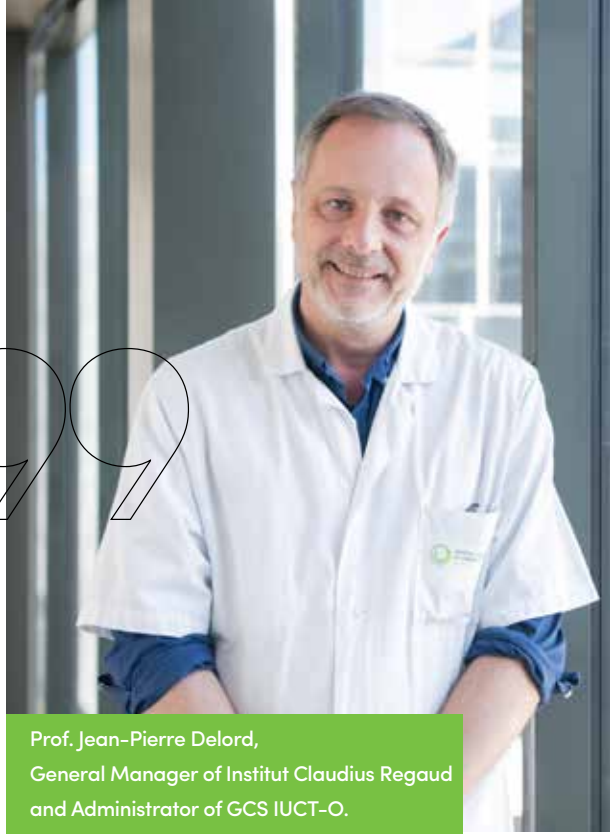
The priorities of the OECI are also reflected in its working groups: accreditation, biobanking and molecular pathology, economic impact and evaluation of cancer in European countries, real-life studies, Interdisciplinary Departments of Supportive Care (DISSPO) and patient relations. In all these areas, the Oncopole can learn from others and contribute to their expertise.

Eight years after the report of the interministerial mission "Oncopole de Toulouse", for which you were commissioned, what is your point of view on the current mode of operation and development of the Oncopole?

The major objectives that were set have now been achieved. When we see the level of research, we can consider that this is an example that should be used by other cities.

It is now time to move on to the next stage, by becoming the conductor of a regional network "orchestra" bringing together all of the structures in the area.

Innovation is born of each one's engagement



Prof. Jean-Pierre Delord,
General Manager of Institut Claudius Regaud
and Administrator of GCS IUCT-O.

Adaptation, collaboration, innovation: these three pillars sustained the year 2020 that has tested the strength and agility of the IUCT-Oncopole. Professor Jean-Pierre Delord, General Manager of the Institut Claudius Regaud and Administrator of the GCS IUCT-Oncopole for the past year, highlights the outstanding involvement of both care and research teams.

How would you sum up this past year, 2020, marked by an unprecedented health crisis?

In this very particular context, especially during the first lockdown when we simply could not stop our activity, we adapted our offer and organization of care to maintain ongoing treatments and keep in touch with patients. Tele-expertise or tele-consultation proved very useful technical solutions, all the while giving top priority to creating a dedicated hospitalization sector to accommodate patients facing the twofold problem of being treated for cancer and a Covid infection. Here, as in many healthcare facilities, the involvement, the fighting spirit of the healthcare professionals and their ability to quickly reorganize were truly outstanding, and I would like to congratulate them once again. This collective commitment by all of the Oncopole teams has quite simply enabled us to maintain a remarkable level of quality of care in a period of crisis, as stated in the latest Unicancer* Quality and Safety Indicators report, that ranks our center first in terms of satisfaction and experience for patients hospitalized for more than 48 hours.

Has scientific activity slowed down?

As with patient care, we have also managed to maintain the quality of our research activity. The teams were very quick to organize themselves to continue their work. And here again, I want to emphasize how everyone's involvement has been exemplary. As a result, we have been able to increase our scientific output to 782 publications in 2020 (compared with 633 in 2019). Such an increase is a definite indicator of our research teams' commitment and excellence.

What have you learned from this crisis?

Our capacity for innovation. The virus has allowed us to test ourselves, to verify that we are a robust organization, made up of committed and involved teams who know how to work together in patients' interest. For example, 1,500 patients benefited from a clinical trial, i.e., 13.7% of our active file. Major advances, such as the development of the cancer vaccine, have continued, as has the increasing use of "adoptive therapies". In July, we were even awarded the "Comprehensive Cancer Center" certification, the highest level of excellence granted by the Organization of European Cancer Institutes (OECI), recognizing the strong integration of research into care, the comprehensive nature of the treatment provided, and the fact that the Oncopole is a European center of expertise in oncology.

What are your priorities for the months and years to come?

Our roadmap is structured around three priorities: improving the coordination of care pathways, bringing innovation to our patients even more quickly —thanks in particular to early-phase clinical trials— and continuing the ongoing shift to artificial intelligence by strengthening collaboration between hard sciences and experimental sciences. Following this route is essential in the field of health in general, and in oncology in particular. Innovation always comes from agile and fluid collaboration between professionals from all fields. Our proven excellence, our ability to collaborate with the structures of the Toulouse ecosystem that surrounds us (aerospace), all strengthen our attractiveness. For example, Evotec's decision to locate one of its bio-incubators in Toulouse, next to the Oncopole (the other being based in Seattle), is a great sign of confidence. The level of our medical-scientific production is comparable to that of the greatest European centers. Just over six years after the opening of the IUCT-Oncopole, we are taking up the challenge of participating in international competition with constant progress.

* French Comprehensive Cancer Centres (FCCCs) Benchmark 2020 of the Quality and Safety Indicators in Care (IQSS).

Marc Penaud, General Manager of Toulouse University Hospital and President of the IUCT-Oncopole General Assembly.

Innovation and projection

Marc Penaud, General Manager of the Toulouse University Hospital and President of the IUCT-Oncopole General Assembly, looks back on the highlights of the year 2020, during which the foundations for a new dynamic and renewed ambition were laid.

Has Covid had an impact on the activities of the Toulouse University Hospital located on the IUCT-Oncopole site?

We have shown constant concern that cancer patients do not suffer from Covid, either directly or indirectly. Care has been maintained. On the other hand, we noted that, further upstream, diagnostic activities had been postponed —either because the technical diagnostic platforms were restricted, due to Covid, or because of patients' self-censorship. In spite of this, there has been an increase in the activity of the University Hospital within the IUCT-Oncopole, which, as a reminder, brings together on the Langlade site the entire Claudius Regaud Institute and only a part of the University Hospital's cancer activities. Overall, we have an increase of 1.7% between 2019 and 2020 for oncology activity of the University Hospital at the Oncopole, compared with 12.3% between 2018 and 2020.

What specific measures have been taken to protect patients?

The Internal Medicine teams at the IUCT-Oncopole set up an inpatient unit to receive and manage suspected Covid patients. This has helped to maintain the bed capacity of the other on-site units. Our Intensive Care units, including the one on-site, have been working closely together to fan patients out appropriately and thus protect them as much as possible. All the technologies making it possible to follow patients at a distance have been used and were very strongly developed in all fields, with remarkable inventiveness shown on the part of our teams for modalities and indicators of follow-up.

Has medical innovation been slowed down by the crisis?

Innovation has more than ever been the driving force. We have done everything possible to use innovative technologies to provide better patient care. We have continued to develop the highly innovative CAR-T cell technique, with incredible success: out of 17 patients treated, we have seven complete remissions and four partial remissions.

There is innovation, and there is projection. 2020 and 2021 are crucial years for drafting the medico-scientific project to structure the coming years around the theme of healthy aging. Better prediction, better identification upstream of all the determinants of pathology, launching more preventive actions, all supported by cutting-edge research to project us into tomorrow's health. The decision taken —extremely important for the future of the Toulouse site— has been to link the Inspire project led by Professor Bruno Vellas with the IUCT-Oncopole. The building project of the Oncopole extension, providing for a common space dedicated to prevention, will make the Toulouse site an outstanding one.

What ambitions will shape the coming years?

First of all, a much stronger structuring of public oncology. To this end, we set up a Federation of Public Oncology within the Toulouse University Hospital, under the very effective leadership and co-leadership of Professor Julien Mazières and Professor Charlotte Vaysse. This federation, working hand in hand with the ICR, is a source of clarity, coherence and harmonization in cancer care in terms of treatment, training, research and organization.

What are the next steps?

At the end of 2020/beginning of 2021, we undertook the operational steps that to launch the extension of the IUCT-Oncopole. This new building will accommodate tertiary activities and allow us to expand in situ the capacity for intensive care, surgery and hospitalization, particularly in Hematology.

The Oncopole site won accreditation from the OECI (Organisation of European Cancer Institutes). We are now in the midst of certifying our network, the first of its kind in the world. This very important step will offer us worldwide visibility on the quality of our processes and care, especially with our industrial partners. It is this quality that has been identified in public and semi-public oncology in Toulouse, and it is this ensemble that we have the reasonable ambition of raising to a national level and, in many areas, well beyond.

Turning crisis in opportunity

Prof. Gilles Favre.

Professor Gilles Favre, Director of the CRCT, and his teams have managed to overcome the constraints of the health crisis. For the Research Center, 2020 marks the renewal of the certification by Inserm and the University Toulouse III-Paul Sabatier, a first accreditation by the CNRS, renewal of the TOUCAN LabEx, creation of a joint laboratory with IRIT and the signing of a first ERC Synergy contract.

2020 has seen a major health crisis. What was the impact of this crisis on the CRCT's activities?

The first lockdown was a shock, which forced us to shut down almost completely and to set up a continuity plan. We were able to maintain a high level of activity and catch up for lost time, thanks to the extension of our contracts with industrial and charitable partners, and our doctoral students, combined with the strong involvement of our teams.

What will remain of this crisis?

In Mandarin Chinese, crisis and opportunity are notions defined by the same word. We have never published so much: 420 articles in 2020. And we have never published so well: for the first time, nearly 20% in high-impact journals. Our researchers have proven their resilience, being able to adapt and take advantage of teleworking to finalize articles in progress. I hope that this solidarity, which has been truly evident, will continue. The opportunity of this crisis is also to have highlighted RNA therapeutics. This large-scale use with the coronavirus vaccine of a technology that we have been using for a long time is indeed unprecedented and has paved the way for new strategies.

What were the highlights of the year?

In addition to the OECI certification, the CRCT obtained the renewal of its Inserm-University Toulouse III-Paul Sabatier certification for five years. And for the first time, CNRS accreditation for all of the teams: we are now an Inserm/University/CNRS Joint Research Unit, with access to calls for tenders and recruitment of CNRS researchers.

At the CRCT, we have set up a team from the Toulouse Institute for Computer Research (IRIT) to develop projects in artificial intelligence around the four main aspects of our research. Working in tandem with CRCT researchers, six IRIT researchers thus form a joint laboratory, allowing us to welcome interns from the prestigious École Polytechnique and the École Centrale Paris.

We signed our first ERC (European Research Council) Synergy contract: this grant, conferred only on exceptional researchers, was awarded to Salvatore Valitutti, who is studying the relationship between T lymphocytes and tumor cells in collaboration with three international laboratories. This 10-million-euro contract, including more than 2.5 million euros for the Center, creates a strong dynamic —we have already submitted three new applications this year.

We have obtained the renewal of our TOUCAN LabEx for a period of four years as well as the creation of a University Research School (EUR). Offering a graduate program, —CARe, Cancer, Aging and Rejuvenation— it was set up in collaboration with the Inspire project, a research laboratory in gerosciences directed by Professor Bruno Vellas. This is a further opening towards technologies of the future and the integration of disciplines such as physics and computer science.

What will be the priorities in the coming years?

This year, 2021, we celebrate the 10th anniversary of the CRCT, and can measure the progress we have made. We have reached a key stage in our development and, in a motivating context very much shared with the Oncopole, are in the process of changing levels in terms of visibility, credibility and scientific power. Obtaining more and more ERC grants, in particular, by supporting applications through a mentorship program is a real objective for us. Finalizing our exchanges with the Systems Analysis and Architecture Laboratory (LAAS), along the lines of our collaboration with IRIT, is another objective. We also plan to recruit a new team to strengthen our ongoing work on metabolism. Exceptional results up until now may well make this theme an element of differentiation. Toulouse is a pioneer in this field.

HIGHLIGHTS OF 2020

JANUARY

Accreditation of Hematology-Transplant

The Hematology-Transplant Department of the IUCT-Oncopole obtains the European JACIE (ISCT-EBMT Joint Accreditation Committee) accreditation for four years.

MARCH

Beginning of the Covid-19 health crisis

A strict lockdown is declared for the whole of France. At the IUCT-Oncopole, a dedicated Covid organization is set up within a week, coordinated with the Toulouse University Hospital. The entire staff rallies to maintain secure care for patients.

MAY

Virtual participation in ASCO

For the first time, the Congress of the American Society for Medical Oncology is held in a 100% digital format. Among the 29 participants from the IUCT-Oncopole and the CRCT: Vera Pancaldi, leader of the CRCT NetB(IO)2 team, presents the "Cancer and Covid-19" international study in a clinical symposium.

FEBRUARY

The 3rd edition of the Toulouse Onco Week

More than 350 researchers participated in the scientific sessions of the TOW that took place from February 1st to 5th. The Onco Run charity race, the Onco Snow village and the public lecture drew more than 7,500 participants.

Handicap and cancer

The IUCT-Oncopole is a laureate in the INCa "Handicap and cancer" call for projects. The project is carried out together with the ASEI (Act, Care, Educate, Integrate) association.

APRIL

Appointment

Prof. Jean-Pierre Delord is appointed General Manager of Institut Claudius Regaud for five years and becomes Administrator of GCS IUCT-Oncopole.


santé

À l'Oncopole, le Pr Delord nommé directeur général

JUNE

Pharmacy almost entirely certified

The Pharmacy renews its ISO 9001:2015 certification for five out of six sectors, maintaining its leadership in this field (1st ISO 9001:2015 certification in France for preparing chemotherapies and managing clinical trials).

JULY

Certified Comprehensive Cancer Center

The IUCT-Oncopole is awarded the highest level of excellence granted by the Organisation of European Cancer Institutes (OECI). This certification pays tribute to the Oncopole for its strong integration of research into patient care as well as its global approach to treatment.

SEPTEMBER

A state-of-the-art accelerator

The Radiotherapy Department receives a new apparatus, Halcyon. The radiotherapists now have access to the whole range of state-of-the-art technologies (arc therapy, stereotaxy, re-irradiation, adaptive radiotherapy, hypofractionation).

NOVEMBER

The CRCT obtains an ERC Synergy Grant

The European Research Council Synergy Grant is awarded to a consortium of four European teams, including that of Salvatore Valitutti (CRCT), for a period of six years. The "ATTACK" project focuses on a new weapon in the tactical arsenal of T cells to destroy tumor cells.

AUGUST

Health Data Hub

The APRIORICS project numbers among the ten laureates of the 2nd call for projects of the Health Data Hub. Under the leadership of Dr. Camille Franchet, for the Toulouse University Hospital, the project uses artificial intelligence (AI) to describe breast tumors as precisely as possible.

OCTOBER

BIOFISS

The BIOFISS project, led by Dr. Agnès Dupret-Bories, receives French National Research Agency (ANR) funding of 724k€. Designed in collaboration with two Inserm (National Institute for Health and Medical Research) laboratories and two industrial partners, it will enable the development of a new biomaterial capable of avoiding salivary fistulae, common in laryngectomized patients after head and neck cancer.

DECEMBER

Renewal of CRCT team certification

For the 2021-2025 term, the CRCT teams up for certification renewal are all very highly rated by the French High Council for Evaluating Research and Higher Education (Hcéres), thus being certified at the same time by Inserm, the Nathional Center for Scientific Research (CNRS) and the University of Toulouse III-Paul Sabatier.

Virtual ASH

Twenty hematologists from the IUCT-Oncopole participate in the 62nd Congress of the American Society of Hematology (ASH), presenting 47 papers.

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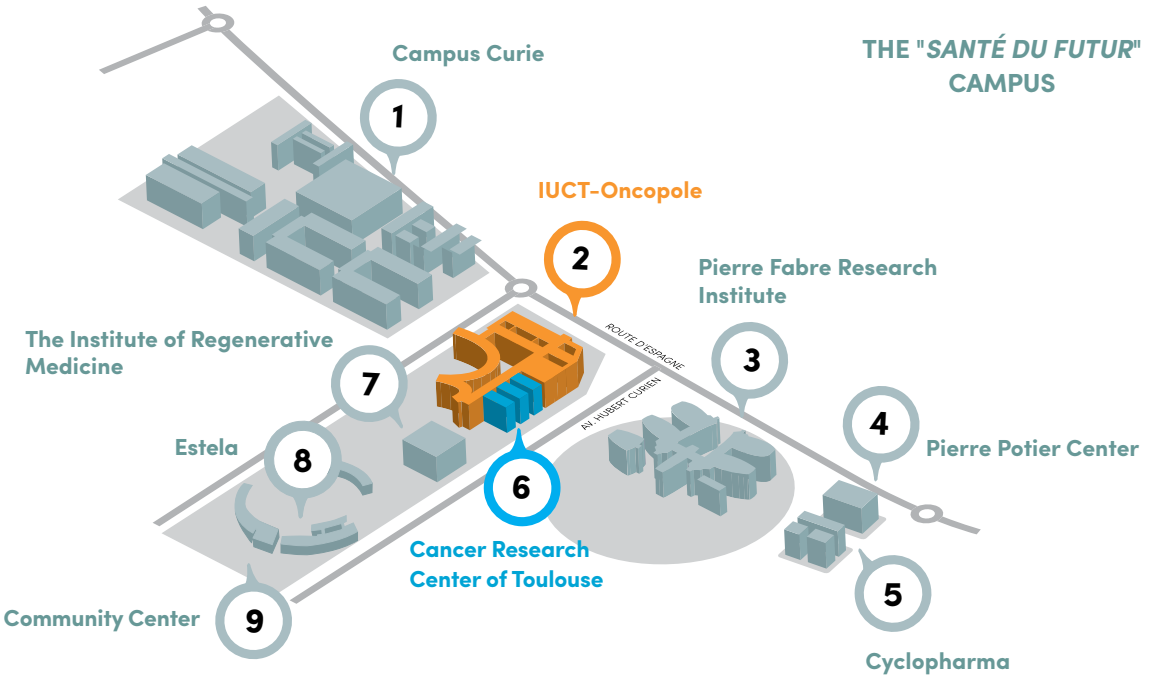
A LEADING PLAYER AT THE HEART OF NETWORKS

A single site

"*Santé du Futur*" is a 220-hectare campus centered round the IUCT-Oncopole hospital and the Cancer Research Center of Toulouse (CRCT). Every day, more than 4,000 professionals from the private and public sectors, representing an exceptional concentration of academic, scientific, medical, clinical and industrial expertise, come together to work towards the same objective – drive back cancer.



In July 2020, the Evotec group, specializing in research and drug discovery, purchased the Sanofi Biopark. Now known as ***"Campus Curie"***, it numbers 600 employees, with 200 more jobs to be created in 2021.

On the other side of the campus is the **Pierre Fabre Research Institute (IRPF)**. In 2019 the IUCT-Oncopole and the CRCT signed a pluriannual agreement for a public-private strategic alliance focusing on developing new alternative personalized therapies.

The Pierre Potier Center, the first building to break ground after the AZF explosion, hosts a business incubator dedicated to biotechnologies and managed by the Toulouse Metropolitan Council. Twelve businesses were housed in 2020, representing 58 jobs. The aim is to host 18 to 20 businesses by the end of 2022, then 25 to 30 companies in 2023-2024.

The Institute of Regenerative Medicine (INCERE) brings together academic researchers and a private structure, the CellEasy start-up. In 2020, the Stromlab laboratory, at the heart of INCERE, expanded to become the **RESTORE Joint Research Unit** (Inserm, CNRS, UT3, EFS, ENVT). Specialized in gerosciences and regenerative medicine, it draws together teams with research orientations going beyond biology alone to include mathematics or AI.

Near the IUCT-Oncopole, a **Community Center** (the *Maison Commune*) offers various services to patients (the departmental branch of the Ligue contre le cancer, a specialized hair dressing salon, specifically designed physical activities developed with CAMI Sport & Cancer, etc.).

Finally, since last year, the **Estela Clinic** has welcomed patients for follow-up care and rehabilitation. In order to guarantee continuity of treatment for cancer patients, the IUCT-Oncopole signed a partnership agreement to provide training for the clinic's healthcare professionals.

In the age of sustainable development

Built on old brownfield land, the Campus is gradually being incorporated into Toulouse Metropolitan Council's sustainable development dynamic. A greenway along the Garonne River provides a traffic-free route to the city center for pedestrians and cyclists.
Furthermore, the largest urban solar power plant in France, with 35,000 solar panels, began operating in October 2020. Endorsed by the *Architectes et Bâtiments de France*, the plant was designed as Land Art, with a pixelized image seen from the sky. It produces the equivalent of electric consumption for 3,000 inhabitants. Initiatives taken by the IUCT-Oncopole itself also include using eco-grazing to maintain the lawns —six Castillonnaise sheep have grazed on 3,000 m² of grass since 2017— and installing beehives on the building's roofs that produce between 30 and 50 kg of honey per year.

... and state-of-the-art innovation in urban mobility!

Work on the new *Téléo Téléphérique*, the urban cable car, began in September 2020. It will whisk passengers in just 10 minutes from the IUCT-Oncopole to the University of Toulouse III–Paul Sabatier, stopping at the Rangueil University Hospital. Due to open by the end of 2021, it will be France's largest urban cable car.
At the same time, test began in the fall of 2020 of the autonomous shuttle EasyMile. In 2021, it will transport users of the site from the parking lots to the IUCT-Oncopole, all along Avenue Irène Joliot-Curie, accompanied by an on-board security operator. A partnership with Alstom, however, plans for "life-size" piloting of a truly autonomous system, with no security operator, in the next few years —a major first in France.

3,000 m² of landscaped areas are accessible to patients and visitors.

Structure

Combining their strengths, the Institut Claudius Regaud and the Toulouse University Hospital's oncology departments provide comprehensive and innovative public-sector cancer care, divided, with no overlap, between three sites: IUCT-Purpan, IUCT-Rangueil/Larrey, and IUCT-Oncopole.

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE
Oncopole

- Hematology
- Women's cancers
- Urologic cancers (medical and innovative radiotherapy)
- Head and neck cancers
- Skin cancers: melanomas
- Sarcomas
- Neuro-oncology
- Thyroid cancers and neuroendocrine tumors
- Oncogenetics
- Geriatric oncology (shared department)
- Pediatric oncology (shared department)
- Radiotherapy
- Nuclear medicine and brachytherapy
- Pathology laboratory
- Onco-hematology laboratory
- Oncology medical biology laboratory

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE
Purpan

- Bone cancers
- Neuro-oncology
- Geriatric oncology (shared department)
- Pediatric oncology (shared department)
- Maxillofacial cancers
- Center for reproductive medicine

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE
Rangueil - Larrey

- Digestive cancers
- Thoracic cancers
- Thyroid cancers
- Head and neck cancers: salivary glands, sinuses, base of the skull
- Urological cancers: prostate, bladder, kidneys
- Reconstructive surgery and rehabilitation

GLOSSARY OF FREQUENTLY USED TERMS

Oncopole: Term used by patients, the general public and the OECI to designate the IUCT-Oncopole and the CRCT.

IUCT-Oncopole: the healthcare consortium (*Groupement de Coopération Sanitaire* - GCS) set up under private law as an equal partnership between the Institut Claudius Regaud and the Toulouse University Hospital.

IUCT: a public interest group (*Groupement d'Intérêt Public* - GIP) comprising all of the area's cancer treatment, research and training establishments, together with the Toulouse Metropolitan Council, the *Oncomip* network (now *Onco-Occitanie*), the *Ligue contre le cancer* and the *Fondation Toulouse Cancer Santé*.

Care-research continuum

The physical proximity of the IUCT-Oncopole's healthcare units and the CRCT's research teams – embodied by the walkway between the two buildings – is a key factor in the Oncopole's success, as it facilitates exchanges all along the "care-research continuum". It also means that the two entities can share technical and support services, including:

- **A Technology Cluster** (manager: Dr. F. Lopez)
- **A Preclinical Trials Center** - CREFRE-US006 (director: Dr. M. Bardotti)
- **A Pathology Laboratory** (manager: Prof. P. Brousset)
- **An Onco-Hematology Transfer Platform** (manager: Prof. E. Delabesse then Dr. V. De Mas)
- **An Oncology Medical Biology Laboratory** (manager: Prof. G. Favre)
- **A Cancer BioBank Center (CRB) - cancer** (manager: Prof. A. Gomez-Mascard)
- **A Biopathology Clinical Trials Support Unit** (SBEC) (manager: Prof. P. Rochaix)
- **A Pharmaceutical Clinical Research Unit** (manager: Dr. A. Grand)

THE IUCT-ONCOPOLE GCS AND ITS SCIENTIFIC COUNCIL

The IUCT-Oncopole GCS is a healthcare consortium (*Groupement de Coopération Sanitaire*) set up under private law and with the Institut Claudius Regaud (ICR) and Toulouse University Hospital as equal partners. The General Manager of the Toulouse University Hospital serves as President of the IUCT-Oncopole General Assembly, and the General Manager of the ICR, as Administrator of the GCS. Internal rules of procedure specify the distribution of disciplines and competences, the governing bodies and the operating modes of the main technical and logistics activities of the site.

L'Etablissement Français du Sang -EFS (French National Blood Service)

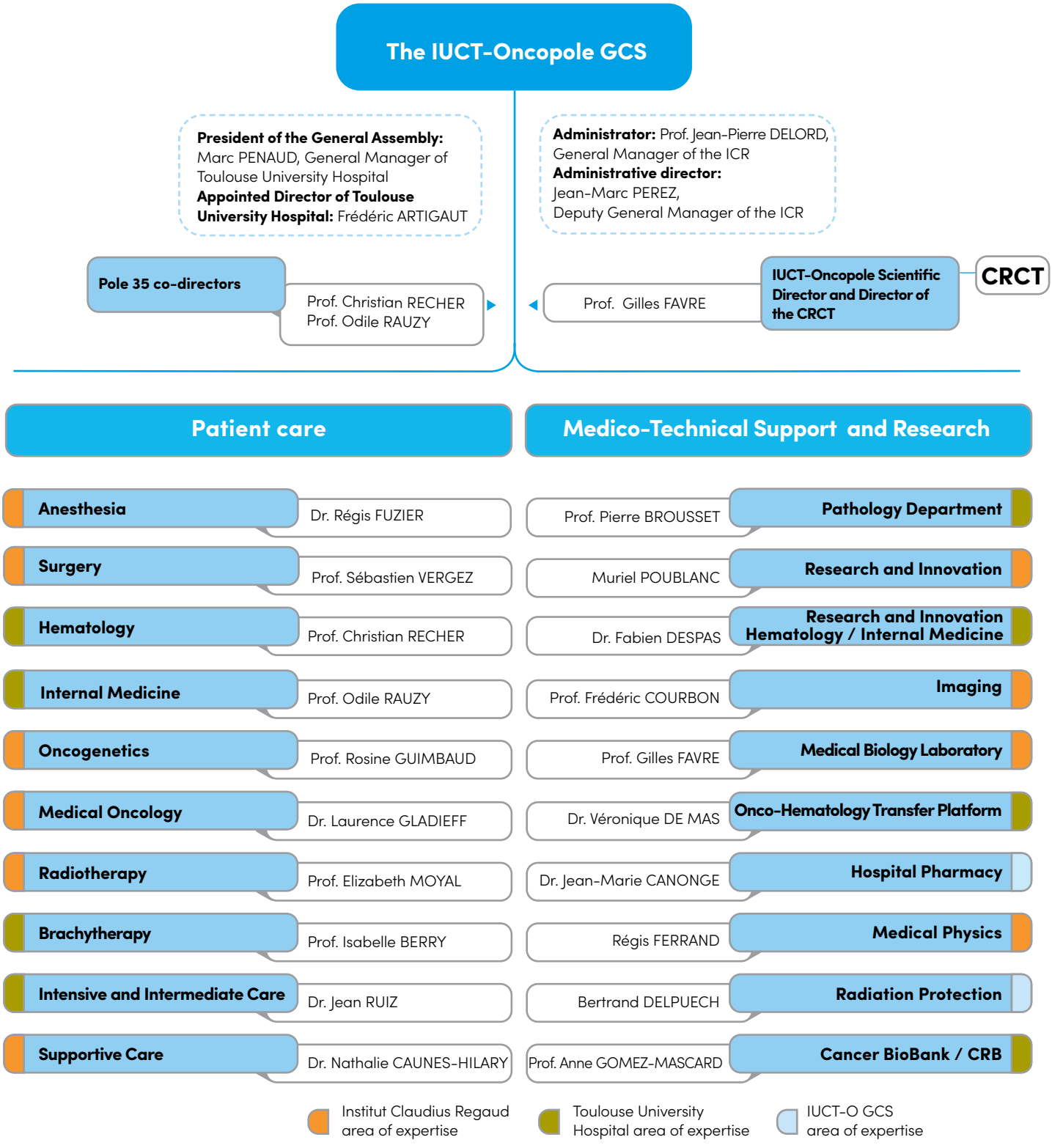
The French National Blood Service has several facilities on the Oncopole site, including:

- a unit for sampling hematopoietic stem cells (HSC) from adults to meet the needs of the IUCT-Oncopole.
- a cellular therapy unit to prepare and store bone marrow and stem cell samples to respond to requests from other centers in the region, France and abroad.

Both units work closely with clinicians and pharmaceutical companies to roll out CAR-T cell therapy.
The French National Blood Service also manages the Institute of Regenerative Medicine (INCERE).
>>>> https://www.efs.sante.fr

ENHANCED ON-SITE GOVERNANCE

A joint Scientific Directorate for the hospital and the CRCT, as well as a Scientific Council, work in concert to oversee the governance of the site. All translational research programs are steered jointly by a physician and a researcher.


The IUCT-Oncopole GCS
President of the General Assembly: Marc PENAUD, General Manager of Toulouse University Hospital
Appointed Director of Toulouse University Hospital: Frédéric ARTIGAUT
Administrator: Prof. Jean-Pierre DELORD, General Manager of the ICR
Administrative director: Jean-Marc PEREZ, Deputy General Manager of the ICR
Pole 35 co-directors
Prof. Christian RECHER
Prof. Odile RAUZY
Prof. Gilles FAVRE
IUCT-Oncopole Scientific Director and Director of the CRCT
CRCT
Patient care
Medico-Technical Support and Research
Anesthesia
Dr. Régis FUZIER
Surgery
Prof. Sébastien VERGEZ
Hematology
Prof. Christian RECHER
Internal Medicine
Prof. Odile RAUZY
Oncogenetics
Prof. Rosine GUIMBAUD
Medical Oncology
Dr. Laurence GLADIEFF
Radiotherapy
Prof. Elizabeth MOYAL
Brachytherapy
Prof. Isabelle BERRY
Intensive and Intermediate Care
Dr. Jean RUIZ
Supportive Care
Dr. Nathalie CAUNES-HILARY
Prof. Pierre BROUSSET
Pathology Department
Muriel POUBLANC
Research and Innovation
Dr. Fabien DESPAS
Research and Innovation Hematology / Internal Medicine
Prof. Frédéric COURBON
Imaging
Prof. Gilles FAVRE
Medical Biology Laboratory
Dr. Véronique DE MAS
Onco-Hematology Transfer Platform
Dr. Jean-Marie CANONGE
Hospital Pharmacy
Régis FERRAND
Medical Physics
Bertrand DELPUECH
Radiation Protection
Prof. Anne GOMEZ-MASCARD
Cancer BioBank / CRB
Institut Claudius Regaud area of expertise
Toulouse University Hospital area of expertise
IUCT-O GCS area of expertise

Clinical departments

The IUCT-Oncopole has 18 departments.

Reception-consultation
Dr. Jérôme Sarini

Medical Oncology
Dr. Laurence Gladieff

Supportive Care
Dr. Nathalie Caunes-Hilary

Oncogenetics
Prof. Rosine Guimbaud

Surgery
Pr. Sébastien Vergez
assistant head:
Dr. Alejandra Martínez

Hematology
Prof. Christian Récher

Internal Medicine
Prof. Odile Rauzy

Brachytherapy
Prof. Isabelle Berry

Medical Imaging
Prof. Frédéric Courbon
assistant head:
Prof. Nicolas Sans

Radiotherapy
Prof. Elizabeth Moyal

Anesthesia
Dr. Régis Fuzier
assistant head:
Dr. Geneviève Salvignol

Pathology
Prof. Pierre Brousset
assistant heads:
Dr. Philippe Rochaix
Prof. Emmanuelle Uro-Coste

Medical Physics
Régis Ferrand

Hospital Pharmacy
Dr. Jean-Marie Canonge
assistant head:
Dr. Florent Puisset

Cancer BioBank / CRB
Prof. Anne Gomez-Mascard

Intensive Care
Dr. Jean Ruiz

Hematology Laboratory
Dr. Véronique De Mas

Medical Biology Laboratory
Prof. Gilles Favre

Local and regional networks

La Fondation Toulouse Cancer Santé (FTCS)

The Fondation Toulouse Cancer Santé-Innabiosanté was set up to promote research and improve knowledge in the field of healthcare technology, especially in relation to cancer. Founded by Amgen, GSK GlaxoSmithKline, Pierre Fabre, Siemens, Total and the Institut Claudius Regaud, it was awarded "public utility" status by ministerial decree on May 5, 2006. The FTCS's main mission is to support the IUCT's scientific projects through annual competitive grant schemes to fund innovative, interdisciplinary and collaborative projects. Calls for proposals are designed to encourage research teams to present the sort of high-risk projects that often lead to tomorrow's scientific, technological and economic breakthroughs.

>>> https://www.toulousecancer.fr/
www.arbredesdonateurs.fr

THE FTCS AND THE GIP IUCT RELY ON THE SAME SCIENTIFIC COUNCIL:

- **François Berger –** Université Joseph Fourier – Grenoble
- **Suzette De La Loge –** Gustave Roussy - Paris
- **Gillies Mc Kenna –** CRUK Oxford - UK
- **Frédérique Penault-Lorca –** CLCC Jean Perrin - Clermont Ferrand
- **Jacques Pouyssegur –** IRCAN – Nice / Monaco
- **Eric Solary –** Gustave Roussy - Paris
- **Alfonso Valencia –** Barcelona Supercomputing Center - Espagne
- **Benoit Van Den Eynde -** Ludwig Institute - UC Louvain - Belgique

The IUCT public interest group (GIP)

The IUCT's collaborative dimension officially came into being via the creation of a public interest group GIP IUCT. Currently presided by Prof. André Syrota, the IUCT GIP unites all of the area's cancer treatment, research and training establishments, including the *Institut Claudius Regaud, the Toulouse University Hospital, the Midi-Pyrénées public-sector cancerology GCS, the Midi-Pyrénées private-sector cancerology GCS, Inserm, the CNRS and the University of Toulouse III–Paul Sabatier,* together with the Toulouse Metropolitan Council, the *Onco-Occitanie* network, the *Ligue contre le cancer* and the *Fondation Toulouse Cancer Santé*.

Onco-Occitanie

Faced with the difficult context imposed by Covid-19, the *Onco-Occitanie* network has fulfilled its missions of coordinating cancer treatment on a regional level, distributing reference documents and follow-up protocols and supporting the region's healthcare professionals: accessing information, disseminating recommendations, proposing a digital organization guide for Multidisciplinary Team (MDT) meetings and implementing an impact study on Cancer and Covid. In parallel, it has continued developing projects in collaboration with the IUCT-Oncopole, accrediting 13 "IUCT" referral MDTs, including three inter-regional teams, that have reviewed 1,990 cases (compared with 1,049 in 2019). It has also facilitated access to CAR-T cell therapy (see p. 49), participated in developing national referentials for head and neck cancers (see p. 58), made virtual reality masks available to young patients (the AJAMIP project (see p. 64) and developed a testicle MTD (see p. 64). The geriatric oncology MOOC, launched in 2019, has confirmed its attractiveness, registering 1,794 participants in 2020 (see p. 84).

>>> www.onco-occitanie.fr

ONCODIETS

Since its creation in 2019, the IUCT-Oncopole has been part of ONCODIETS, the first network of independent cancer nutrition specialists in partner French Comprehensive Cancer Centers (CLCCs). This network aims to ensure the continuity of care for patients when they leave the hospital.

GENEPY

GENEPY is a cancer care network for people in the Midi-Pyrénées area who have a genetic predisposition to breast, ovarian, colorectal or endometrial cancer. Set up with support from the *Institut national du cancer* (INCa) and run by the Oncogenetics Organ Coordination Committees, GENEPY facilitates and coordinates genetic screening, in line with INCa guidelines, to ensure that every patient receives the best possible care.

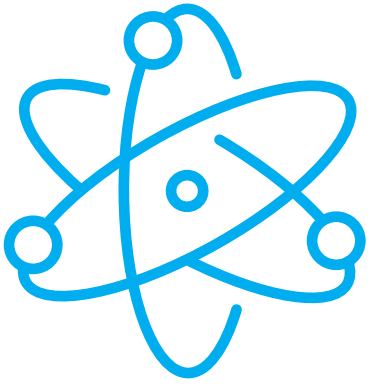
Cancéropôle Grand Sud-Ouest (GSO)

Cancéropôle GSO is a dynamic cancer research network of almost 500 scientific and medical research teams, from Bordeaux, Limoges, Nîmes, Poitiers and Toulouse, that work together on a wide variety of collaborative projects. It provides funding for promising projects in the fight against cancer and organizes numerous scientific events.

>>> http://www.canceropole-gso.org/

A "CITY-HOSPITAL" LIAISON SYSTEM UNDER TEST

The General Medicine Department, Medical Oncology Department, Onco-Occitanie regional cancer network and the Occitanie Regional Health Agency are working together to improve treatment pathways for patients with metastatic solid tumors by facilitating communication between family doctors and hospitals. To do this, they have developed a strategy centered around structured "return home" consultations, conducted in conjunction with the patient's family doctor. These consultations are coordinated by general practitioners having completed a special program in cancer treatment (DESC). The IUCT-Oncopole is currently testing the system with one of the five newly trained physicians. Baptized CREDO, the liaison system aims to make it easier for caregivers to share information to help them anticipate patients' needs and thereby reduce unplanned visits to specialist healthcare centers. As a result, patients should be able to remain in their own "healthcare areas" without compromising the quality of care. Supervised by Prof. M-E. Rougé-Bugat, and funded by the DGOS, it is now functioning and already includes 660 patients (with plans to involve 825).



National networks

The IUCT-Oncopole, through the Institut Claudius Regaud and Toulouse University Hospital, is a member of Unicancer and the *Fédération Hospitalière de France* (FHF). It is heavily involved in several of Unicancer's specialist working groups. Prof. J-P. Delord is vice-president of the Immuno-oncology Group (GIO), created in December 2016, and a member of Scientific and Strategic Council.

The IUCT-Oncopole is a *"Centre expert régional"*, one of eight INCa-accredited networks:

- **CARADERM:** Rare skin cancers (contact: Prof. N. Meyer)
- **CARARE:** Rare kidney cancers (contact: Dr. C. Chevreau)
- **NETSARC**: Sarcomas (contact: Dr. C. Chevreau)
- **POLA**: High-grade oligodendrogliomas (contact: Prof. E. Moyal)
- **REF-COR**: Rare head and neck cancers (contact: Prof. S. Vergez)
- **RENAPE**: Rare peritoneal cancers (contact: Dr. G. Ferron)
- **TMRG**: Rare gynecological malignancies (contact: Dr. G. Ferron)
- **TUTHYREF**: Refractory thyroid cancers (contact: Dr. S. Zerdoud)

It is a regional pathology center for four rare cancers:

- **LYMPHOPATH**: Lymphomas (contact: Prof. P. Brousset)
- **MESOPATH**: Malignant pleural mesotheliomas and rare retroperitoneal tumors
- **RRePS**: Soft tissue and visceral sarcomas
- **TENpath**: Rare neuroendocrine tumors (contact: Dr. M. Danjoux)

The IUCT-Oncopole is also a member of four INCa-accredited research networks:

- **CLIP²**: Early phase clinical trials centers (contact: Prof. J-P. Delord)
- **ARCAGY-GINECO**: National investigation group for the study of ovarian and breast cancers (contact: Dr. L. Gladieff)
- **LYSA**: Collaborative clinical and translational research group on lymphoma (contact: Prof. C. Laurent)
- **RADIOTRANSNET**: Preclinical radiotherapy research in France (contact: Prof. E. Moyal)

A partner in creating the French Society for Gynecological Oncology (SFOG) Campus

Under the auspices of the SFOG, the Campus SFOG group came into being May 12, 2020. This group of young physicians constitutes a network of professionals, encouraging dialogue among young practitioners to foster a global and multimodal approach to oncological gynecology. Dr. L. Gladieff is one of the founding members.

European and international networks

The IUCT-Oncopole has an international outlook and is a founding and/or active member of several European and global networks.

Organisation of European Cancer Institutes (OECI)

Since 2018 the IUCT-Oncopole has been a member of the OECI Comprehensive Cancer Center network whose mission is to create a critical mass of expertise and competences to support the development of personalized care. Nearly 100 members, 11 of whom are French, work together to offer patients all across Europe access to the best possible care. An accreditation process was begun in 2019, together with the CRCT, resulting in an audit by seven OECI experts. In 2020, the IUCT-Oncopole was awarded Comprehensive Cancer Center certification. This designation honors the strong integration of research and patient care as well as the global nature of care at the Oncopole. It testifies to international recognition.

With the OECI experts.

European Neuroendocrine Tumor Society (ENETS)

The IUCT-Oncopole and the IUCT-Rangueil/Larrey have been certified by the European Neuroendocrine Tumor Society (ENETS) as the "University Center of Excellence for Neuroendocrine Tumors, Toulouse". Led by Prof. R. Guimbaud and Dr. L. Dierickx, the fruitful result of this application process recognizes the center's multidisciplinary expertise in recruitment, diagnosis, treatment, clinical research and training doctors in a rare pathology - digestive neuroendocrine tumors. Only three centers in France have been thus accredited in France.

OncoDistinct

The IUCT-Oncopole is part of the OncoDistinct international clinical research network. Launched in 2015, OncoDistinct now has 27 members, including 12 Comprehensive Cancer Centers and 16 university hospitals. Dr. Carlos Gomez Roca is part of the coordinating team. The network promotes innovative, multi-center studies aimed at accelerating the development of anticancer drugs, especially for conditions where no therapeutic standard exists yet. In this context, the IUCT-Oncople is actively participating in two trials sponsored by the network: MiMe (Principal investigator: Dr. Carlos Gomez Roca) and Brainstorm (Principal investigator: Dr. Eleonora de Maio).

European Network for Cutaneous ADverse events to Oncologic drugs (ENCADO)

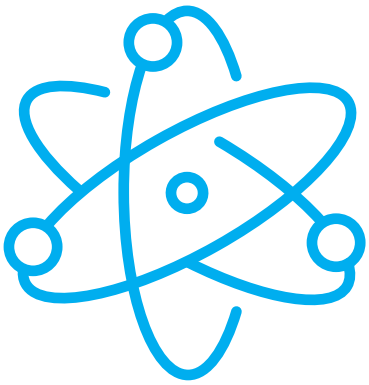
This European network came into being on the initiative of Dr. V. Sibaud with the collaboration of Prof. G. Fabbrocini (Naples University Hospital Federico II) and Dr. A. Freites-Martinez (Fuenlabrada Madrid University Hospital). It groups together more than 60 members from 15 European countries. Dr. E. Vagarios is responsible for coordinating the oral toxicity section. Two projects have been published in international journals in 2020: the characterization of anticancerous immunotherapy-induced psoriasis and a description of vitiligoid reactions from anti-CDK 4/6 (ribociclib, palbociclib). A study has also been undertaken on European recommendations on dermatologic toxicities from immune checkpoint inhibitors.

European Society of Gynaecological Oncology (ESGO)

The IUCT-Oncopole has been a European Society of Gynaecological Oncology (ESGO) accredited training center since 2017. The first two diplomas have since been awarded to Dr. C. Martinez Gomez and Dr. M-A. Angeles. Only seven other centers in France are accredited to provide this high-level training.

Catalonia-Occitanie Oncology Group (GOCO)

This association of radiotherapy physicians, physicists, technicians and nurses in Catalonia and Occitanie was set up to promote disciplines relating to oncology, to offer initial and continuing training, and to encourage inter-professional exchanges. To this end, GOCO draws up standardized diagnosis protocols and develops collaborative research projects.



II

BASIC AND TRANSLATIONAL RESEARCH

Presentation of CRCT

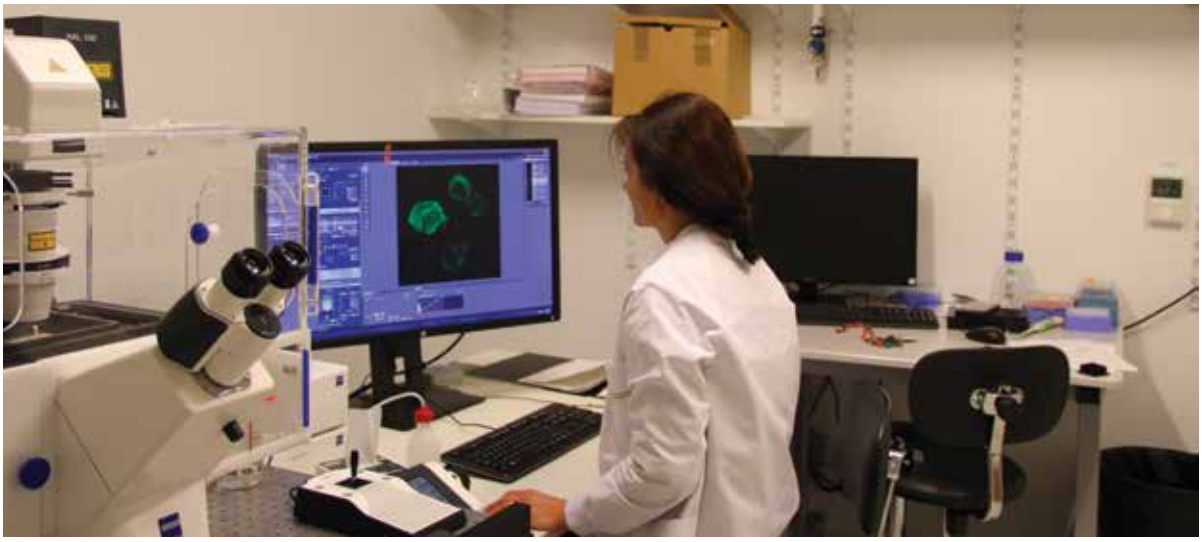
The year 2020 was marked by the five-year evaluation of the CRCT by its supervisory authorities. Its activity and strategic plan for 2021-2026 brought renewal of its Inserm and University of Toulouse III-Paul Sabatier certification, but also CNRS recognition and accreditation for having restructured its project to encompass both basic and translational research. Indeed, starting from 2019, teams began refocusing on existing research themes, encouraging teamwork and professional mobility. The CRCT thus concentrated 21 research teams into 18, one of which was emergent, as of January 1, 2021.

The CRCT, already an Inserm/University of Toulouse III-Paul Sabatier Joint Research Unit (UMR) 1037, also becomes CNRS/University of Toulouse III-Paul Sabatier UMR 5071.

The CRCT remains the only center in Toulouse dedicated entirely to cancer research. The close collaboration with IUCT-Oncopole clinicians allows for transfer of research results to clinical practice and development of innovative approaches in diagnosis and treatments. The CRCT has reinforced its four research themes and two transversal themes:

- Oncogenic signaling, DNA damage and genetic instability
- RNA and cancer
- Tumor microenvironment and metabolism
- Oncoimmunology
- Resistance mechanisms and new targets: from molecular pharmacology to clinical pharmacology
- Development of mathematical, physical and computational approaches in oncology

In accordance with the recommendations of its Scientific council, the CRCT is pursuing its actions to further consolidate its strengths, launch new initiatives, recruit new talents, develop its partnership strategy and improve its visibility and attractiveness.



Cancer Research Center of Toulouse - CRCT

Key figures

18
basic and translational research **teams**

165
researchers, university lecturers and researchers, and clinicians

9
technical support units

33
collections stored in the Cancer BioBank

4 **basic research themes** and **2** integrated research programs

Less than 6 months
to translate a CRCT discovery into a clinical trial at the IUCT-Oncopole

Highlight 2020

Salvatore Valitutti, laureate of an ERC Synergy Grant

Salvatore Valitutti was awarded a prestigious European Research Council (ERC) Synergy grant for the "**ATTACK**" project, with three other partners:
- Jens Reggit (*Center for Integrative Physiology and Molecular Medicine, Saarland University, Homburg, Germany)*
- Cosima Baldari (*Department of Life sciences, University of Siena, Italy*)
- Michael Dustin (*Kennedy Institute of Rheumatology – NDORMS, University of Oxford, United Kingdom*).

The overall budget for the **ATTACK** project **– Analysis of the tactical arsenal of T cells to kill cancer cells —** amounts to 10 million euros over six years.

The Toulouse team, in cooperation with scientists from Oxford University, has identified a previously unknown weapon in the tactical arsenal of T cells involved in the protection against pathogen-infected cells as well as cancer cells: the supramolecular attack particles (SMAPs) that are rapidly released by the CTLs are capable of killing target cells (1). Based on this discovery, a consortium was set up to develop an ambitious research project capable of elucidating this new mechanism for fighting cancer.

The ATTACK consortium works on four research themes to determine i) how SMAPs are generated, ii) how they are released, iii) how they function and iv) how cancer cells react to this attack. If, as hypothesized, SMAPs are autonomous extracellular killing entities capable of releasing a cytotoxic load, it would be possible to design these particles so that they function independently of T cells.
In perspective, new therapeutic approaches can be developed at the Toulouse University Cancer Institute.

1. Balint Š, Muller S, Fischer R, Kessler BM, Harkiolaki M, Valitutti S, Dustin ML. **Supramolecular attack particles are autonomous killing entities released from cytotoxic T cells**. Science. 2020 May 22;368(6493):897-901.

THE CRCT by team

The CRCT has restructured into 18 teams whose research is supported by an on-site, state-of-the-art Technology Center with its own staff.

T2i - Maha Ayyoub / Jean-Pierre Delord

SIGNATHER - Gilles Favre / Olivier Sordet

MELASPHINX - Bruno Ségui / Nathalie Andrieu

RNA_{REG}
Stefania Millevoi

MICROPANC
Corinne Bousquet

R'N Blood
Stéphane Pyronnet / Fabienne Meggetto

NoLymIT
Camille Laurent

ImPACT
Pierre Cordelier

RADOPT - Elizabeth Moyal / Christine Toulas

CMATI - Marc Poirot / Sandrine Silvente-Poirot

GENIM - Hervé Avet-Loiseau / Ludovic Martinet

DIAD
Etienne Chatelut

ALTFAL
Eric Delabesse

SigDYN
Julie Guillermet-Guibert

METAML
Jean-Emmanuel Sarry

ONCOSARC
Frédéric Chibon

DynAct
Salvatore Valitutti

NetB(IO)²
Vera Pancaldi
Chair Pierre Fabre

Technology cluster
Frédéric Lopez

TEAM

ANTITUMOR IMMUNITY AND IMMUNOTHERAPY – T2i

Team leaders: Prof. Maha Ayyoub and Prof. Jean-Pierre Delord

Keywords: T cell antitumor response, tumor antigens, lymphocyte exhaustion, immune checkpoint modulators, anticancer vaccines

Funding sources: CVC (Cancer Research Institute), imCORE (Roche/Genentech), MSDAVENIR, AstraZeneca, BMS, IUCT-Oncopole Translational Research, Ligue contre le cancer

Research theme: An essential step in overcoming tumors' resistance to immunotherapies is deciphering the molecular and cellular mechanisms involved. The team contributes to research in this field by investigating the role of tumor antigen-specific T cell responses in clinical responses to immunotherapies in patients with immune responsive tumors (lung, bladder, and head and neck cancers) treated using immune checkpoint inhibitors. Studies of patients with immune resistant cancers (cervical and ovarian cancers) are used to determine the mechanisms that lead to lymphocyte exhaustion in the tumor microenvironment. Together, these projects contribute to the identification of biomarkers of response to immunotherapy and to the development of combination therapies, in particular of anticancer vaccines that stimulate antitumor T cell responses and immune checkpoint modulators capable of reversing T cell exhaustion at the tumor site.

MAJOR PUBLICATIONS IN 2020

1. Balança CC, Salvioni A, Scarlata CM, Michelas M, Martinez-Gomez C, Gomez-Roca C, Sarradin V, Tosolini M, Valle C, Pont F, Ferron G, Gladieff L, Vergez S, Dupret-Bories A, Mery E, Rochaix P, Fournié JJ, Delord JP, Devaud C, Martinez A, Ayyoub M. PD-1 blockade restores helper activity of tumor-infiltrating exhausted PD-1hiCD39+ CD4 T cells. JCI Insight. 2020;142513.

2. Balança CC, Scarlata CM, Michelas M, Devaud C, Sarradin V, Franchet C, Martinez Gomez C, Gomez-Roca C, Tosolini M, Heaugwane D, Lauzéral-Vizcaino F, Mir-Mesnier L, Féliu V, Valle C, Pont F, Ferron G, Gladieff L, Motton S, Tanguy Le Gac Y, Dupret-Bories A, Sarini J, Vairel B, Illac C, Siegfried-Vergnon A, Mery E, Fournié JJ, Vergez S, Delord JP, Rochaix P, Martinez A, Ayyoub M. Dual Relief of T-Lymphocyte Proliferation and Effector Function Underlies Response to PD-1 Blockade in Epithelial Malignancies. Cancer Immunol Res. 2020 Apr 15.

3. Fluckiger A et al. Cross-reactivity between tumor MHC class I-restricted antigens and an enterococcal bacteriophage. Science. 2020;369:936-42.

4. Martinez A, Delord JP, Ayyoub M, Devaud C. Preclinical and Clinical Immunotherapeutic Strategies in Epithelial Ovarian Cancer. Cancers (Basel). 2020;12(7). pii: E1761.

5. Prat M, Le Naour A, Coulson K, Lemée F, Leray H, Jacquemin G, Rahabi MC, Lemaitre L, Authier H, Ferron G, Barret JM, Martinez A, Ayyoub M, Delord JP, Gladieff L, Tabah-Fisch I, Prost JF, Couderc B, Coste A. Circulating $CD14^{high}$ $CD16^{low}$ intermediate blood monocytes as a biomarker of ascites immune status and ovarian cancer progression. J Immunother Cancer. 2020;8(1):e000472.

6. Trimaglio G, Tilkin-Mariamé AF, Féliu V, Lauzéral-Vizcaino F, Tosolini M, Valle C, Ayyoub M, Neyrolles O, Vergnolle N, Rombouts Y, Devaud C. Colon-specific immune microenvironment regulates cancer progression versus rejection. Oncoimmunology. 2020;9(1):1790125.

TEAM

CANCER CELL SIGNALING, ONCOGENESIS AND THERAPEUTICS – SIGNATHER

TEAM ACCREDITED BY THE FONDATION POUR LA RECHERCHE MÉDICALE

Team leaders: Prof. Gilles Favre and Dr. Olivier Sordet

Keywords: RTK/RAS/ERK, Rho GTPases, genomic instability, transcription, resistance to targeted therapies, split GFP, liquid biopsy, clinical trials, lung cancers

Funding sources: Fondation pour la Recherche Médicale, INCa, Fondation ARC, Fondation de France, Ligue contre le cancer, RNA, AstraZeneca, Inserm Transfert, Occitanie Region

Research theme: The team investigates the mechanisms underlying the deregulation of cell signaling pathways in cancers, in particular receptor tyrosine kinase (RTK) pathways, Rho-GTPase pathways and transcription-related double-strand DNA breaks. By determining the mechanisms involved in resistance to targeted therapies, focusing on RTK/RAS/ERK pathways, and developing innovative biotechnologies, including split GFP and nanobodies, this research will help resolve issues in cell biology and lead to new therapeutic strategies. Bioclinical (liquid biopsies) and clinical studies of lung cancers and melanoma are carried out in collaboration with the IUCT.

MAJOR PUBLICATIONS IN 2020

1. Bousquet Mur E, Bernardo S, Papon L, Mancini M, Fabbrizio E, Goussard M, Ferrer I, Giry A, Quantin X, Pujol JL, Calvayrac O, Moll HP, Glasson Y, Pirot N, Turtoi A, Cañamero M, Wong KK, Yarden Y, Casanova E, Soria JC, Colinge J, Siebel CW, Mazieres J, Favre G, Paz-Ares L, Maraver A. Notch inhibition overcomes resistance to tyrosine kinase inhibitors in EGFR-driven lung adenocarcinoma. J Clin Invest. 2020;130(2):612-24.

2. Cristini A, Gromak N, Sordet O. Transcription-dependent DNA double-strand breaks and human disease. Mol Cell Oncol. 2020;7(2):1691905.

3. Laplagne C, Meddour S, Figarol S, Michelas M, Calvayrac O, Favre G, Laurent C, Fournié JJ, Cabantous S, Poupot M. Vγ9Vδ2 T Cells Activation Through Phosphoantigens Can Be Impaired by a RHOB Rerouting in Lung Cancer. Front Immunol. 2020;11:1396.

4. Guibert N, Pradines A, Favre G, Mazieres J. Current and future applications of liquid biopsy in nonsmall cell lung cancer from early to advanced stages. Eur Respir Rev. 2020;29(155).

5. Mazieres J, Cropet C, Montané L, Barlesi F, Souquet PJ, Quantin X, Dubos-Arvis C, Otto J, Favier L, Avrillon V, Cadranel J, Moro-Sibilot D, Monnet I, Westeel V, Le Treut J, Brain E, Trédaniel J, Jaffro M, Collot S, Ferretti GR, Tiffon C, Mahier-Ait Oukhatar C, Blay JY. Vemurafenib in non-small-cell lung cancer patients with $BRAF_{V600}$ and $BRAF_{nonV600}$ mutations. Ann Oncol. 2020;31(2):289-94.

TEAM

CERAMIDE METABOLISM IN MELANOMAS: FROM BASIC MECHANISMS TO IMMUNOTHERAPY - MELASPHINX

TEAM ACCREDITED BY THE FONDATION ARC

Team leaders: Prof. Bruno Ségui and Dr. Nathalie Andrieu-Abadie

Keywords: Ceramide, sphingosine 1-phosphate, melanoma, oncometabolism, oncoimmunology

Funding sources: Fondation ARC, INCa, Fondation de France, BMS, Fondation BMS, ANR, Era-Net Transcan-2

Research theme: The team evaluates the impact of alterations in ceramide metabolism (i) in initial stages and melanoma progression, (ii) in resistance to immunotherapies targeting immune checkpoints. In this context, the team studies interconnections between TNF signaling and ceramide metabolism, as well as the consequences of associating anti-TNF drugs with immunotherapies, in preclinical models of melanoma and in patients with advanced melanoma. Moreover, our research will evaluate, within the framework of clinical trials, whether TNF and ceramide metabolites may be considered predictive biomarkers of response or resistance to immunotherapies.

In 2020, among the team's publications, two original articles illustrate the possibility of sensitizing melanomas to immunotherapies by reprogramming ceramide metabolism, and a clinical article discusses the first patients included in the TICIMEL clinical trial.

MAJOR PUBLICATIONS IN 2020

1. Montfort A, Filleron T, Virazels M, Dufau C, Milhès J, Pages C, Olivier P, Ayyoub M, Mounier M, Lusque A, Brayer S, Delord JP, Andrieu-Abadie N, Levade T, Colacios C, Ségui B, Meyer N. Combining nivolumab and ipilimumab with infliximab or certolizumab in patients with advanced melanoma: first results of a phase 1b clinical trial. Clin Cancer Res. 2020 Dec 3.

2. Pellerin L, Carrié L, Dufau C, Nieto L, Ségui B, Levade T, Riond J, Andrieu-Abadie N. Lipid metabolic Reprogramming: Role in Melanoma Progression and Therapeutic Perspectives. Cancers (Basel). 2020 Oct 27;12(11):E3147.

3. Carrié L, Virazels M, Dufau C, Montfort A, Levade T, Ségui B, Andrieu-Abadie N. New Insights into the Role of Sphingolipid Metabolism in Melanoma. Cells. 2020 Aug 26;9(9):E1967.

4. Imbert C, Montfort A, Fraisse M, Marcheteau E, Gilhodes J, Martin E, Bertrand F, Marcellin M, Burlet-Schiltz O, Peredo AG, Garcia V, Carpentier S, Tartare-Deckert S, Brousset P, Rochaix P, Puisset F, Filleron T, Meyer N, Lamant L, Levade T, Ségui B, Andrieu-Abadie N, Colacios C. Resistance of melanoma to immune checkpoint inhibitors is overcome by targeting the sphingosine kinase-1. Nat Commun. 2020 Jan 23;11(1):437.

TEAM

RNA-BINDING PROTEINS AND GENOTOXIC STRESS - RNA_{REG}

Team leader: Dr. Stefania Millevoi

Keywords: RNA, post-transcription, autophagy, anticancer therapy

Funding sources: ANR, Ligue contre le cancer

Research theme: The team studies modifications of post-transcriptional gene expression in response to anticancer treatments. Research targets the pertinent molecular mechanisms, the extent of regulations involved on the cellular level, their clinical pertinence for treatment-resistant patients, and finally, their potential targeting to develop innovative strategies based on RNA. In 2020, collaboration with the RADOPT team, as well as with J. Gilhodes from the IUCT-Oncopole's Office of Clinical Trials, further elucidated the central role of RNA binding proteins and RNA structures in glioblastoma resistance to radiochemotherapy.

The team was restructured and reinforced to bring together E. Espinos and S. Manenti, experts in autophagy, and a clinician, a radiotherapy oncologist from the IUCT-Oncopole, to explore RNA biology in Head and neck cancer in response to genotoxic stress. By proving that autophagy was regulated by both small non-coding RNAs and cell cycle regulators, and by elucidating the mechanistic link between autophagy and tumor metabolism, S. Manenti and E. Espinos have stimulated the interest in targeting autophagy as a strategic therapy for patients with, respectively, ALK positive acute myeloid leukemia and anaplastic large-cell lymphoma (ALCL).

MAJOR PUBLICATIONS IN 2020

1. Herviou P, Le Bras M, Dumas L, Hieblot C, Gilhodes J, Cioci G, Hugnot JP, Ameadan A, Guillonneau F, Dassi E, Cammas A, Millevoi S. hnRNP H/F drive RNA G-quadruplex-mediated translation linked to genomic instability and therapy resistance in glioblastoma. Nat Commun. 2020;11(1):2661.

2. Bertorello J, Sesen J, Gilhodes J, Evrard S, Courtade-Saïdi M, Augustus M, Uro-Coste E, Toulas C, Moyal EC-J, Seva C, Dassi E, Cammas A, Skuli N, Millevoi S. Translation reprogramming by eIF3 linked to glioblastoma resistance. NAR Cancer 2020;2.

3. Nowosad A, Jeannot P, Callot C, Creff J, Perchey RT, Joffre C, Codogno P, Manenti S, Besson A. p27 controls Ragulator and mTOR activity in amino acid-deprived cells to regulate the autophagy-lysosomal pathway and coordinate cell cycle and cell growth. Nat Cell Biol. 2020;22(9):1076-90.

4. Bosc C, Broin N, Fanjul M, Saland E, Farge T, Courdy C, Batut A, Masoud R, Larrue C, Skuli S, Espagnolle N, Pagès JC, Carrier A, Bost F, Bertrand-Michel J, Tamburini J, Récher C, Bertoli S, Mansat-De Mas V, Manenti S, Sarry JE, Joffre C. Autophagy regulates fatty acid availability for oxidative phosphorylation through mitochondria-endoplasmic reticulum contact sites. Nat Commun. 2020;11(1):4056.

5. Sorrentino D, Frentzel J, Mitou G, Blasco RB, Torossian A, Hoareau-Aveilla C, Pighi C, Farcé M, Meggetto F, Manenti S, Espinos E, Chiarle R, Giuriato S. High Levels of miR-7-5p Potentiate Crizotinib-Induced Cytokilling and Autophagic Flux by Targeting RAF1 in NPM-ALK Positive Lymphoma Cells. Cancers. 2020;12(10):2951.

6. Cartel M, Mouchel PL, Gotanègre M, David L, Bertoli S, Mansat-De Mas V, Besson A, Sarry JE, Manenti S, Didier C. Inhibition of ubiquitin-specific protease 7 sensitizes acute myeloid leukemia to chemotherapy. Leukemia. Epub 2020 May 23.

TEAM

MICROENVIRONMENT AND THERAPEUTIC RESISTANCE IN PANCREATIC NEOPLASMS - MICROPANC

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leader: Dr. Corinne Bousquet

Keywords: Fibroblasts associated with cancer, protein synthesis, signaling pathways, tumor heterogeneity, intercellular dialogues

Funding sources: Ligue contre le cancer, INCa, Plan Cancer, Fondation ARC

Research theme: The team studies the progression mechanisms and therapeutic resistance of pancreatic ductal carcinoma (PDC), investigating the cellular and molecular mechanisms involved in its aggressiveness. Once identified, these mechanisms are validated in cell models derived from patients' tumors, but also in vivo in models mimicking the pathology in an integrated manner (including patients' macro- and micro-environment/s). The dialogues between tumor cells and cells of the microenvironment are now recognized as essential to tumor cell plasticity. The team is more specifically interested in majority stromal cells —cancer associated fibroblasts (CAF)— in pancreatic cancer, and studies the mechanisms used by the CAFs to develop pro-tumor, protective properties vis-à-vis anticancer agents to co-target vulnerabilities and develop therapeutics. The heterogeneity of CAFs among tumors from different patients, but also within any single tumor, is being analyzed in order to find "personalized" therapies specific to the most dangerous cell populations, depending on the individual patient. In 2020, the team identified two targets responsible for the aggressiveness of PDC via a dialogue between CAF and certain myeloid immune cells, as well as a sub-type of PDC by means of "omics" analyses showing a tumor-stroma metabolic dependency.

MAJOR PUBLICATIONS IN 2020

1. Zaghdoudi S, Decaup E, Belhabib I, Samain R, Cassant-Sourdy S, Rochotte J, Schlaepfer D, Cros J, Neuzillet C, Strehaiano M, Alard A, Tomasini R, Rajeeve V, Perraud A, Mathonnet M, Pearce OMT, Martineau Y, Pyronnet S, Bousquet C*, Jean C*. * co-corresponding. FAK activity in cancer-associated fibroblasts is a prognostic marker and a druggable key metastatic player in pancreatic cancer. EMBO Mol Med. 2020;12(11):e12010.

2. Hilmi M, Nicolle R, Bousquet C, Neuzillet C. Cancer-Associated Fibroblasts: Accomplices in the Tumor Immune Evasion. Cancers (Basel). 2020;12(10):2969. .

3. Shin S, Nicolle R, Jean C, Samain R, Ayadi M, Raffenne J, Brunel A, Solorzano J, Neuzillet C, Joffre C, Rocchi S, Iovanna J, Dusetti N, Larsson O, Pyronnet S, Bousquet C, Martineau Y. (2020) Translatome-based classification reveals a dual metabolic dependency of a new tumor subtype of pancreatic cancer. bioRxiv 2020.12.23.424227;

4. Bosc C, Broin N, Fanjul M, Saland E, Farge T, Courdy C, Batut A, Masoud R, Larrue C, Skuli S, Espagnolle N, Pagès JC, Carrier A, Bost F, Bertrand-Michel J, Tamburini J, Récher C, Bertoli S, Mansat-De Mas V, Manenti S, Sarry JE, Joffre C. Autophagy regulates fatty acid availability for oxidative phosphorylation through mitochondria-endoplasmic reticulum contact sites. Nat Commun. 2020;11(1):4056.

TEAM

BIOLOGY OF RNAS IN HEMATOLOGICAL CANCERS - R'N Blood

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leaders: Dr. Stéphane Pyronnet and Dr .Fabienne Meggetto

Keywords: RNAm, miRNA, lncRNA et circRNA, gene expression, translation, AML and anaplastic large-cell lymphoma, resistance

Funding sources: Ligue Contre le Cancer, LabEx TOUCAN, Fondation Toulouse Cancer Santé, Fondation de France, Fondation ARC, Association Laurette Fugain, Association Eva pour la vie, Occitanie Region

Research theme: The team focuses on molecular mechanisms of RNA-dependent gene regulation (coding mRNAs and non-coding micro-, lnc-, and circRNAs). Explorations are carried out in normal and tumoral hematopoiesis, as well as in therapeutic resistance, focusing on acute myeloid leukemia and anaplastic large-cell lymphoma. In 2020, this new team restructured, to be officially created in January 2021, bringing together researchers and clinicians around a common theme —RNA blood tumors. In 2020, part of the team continued working on pancreatic cancers. Team members contributed to identifying potentially new therapeutic targets for pancreatic cancer and demonstrated that the NPM-ALK oncogene in anaplastic large-cell lymphoma was capable of transforming mature T cells by restoring a progenitor thymic cell phenotype.

MAJOR PUBLICATIONS IN 2020

1. Jaud M, Philippe C, Di Bella D, Tang W, Pyronnet S, Laurell H, Mazzolini L, Rouault-Pierre K, Touriol C. Translational Regulations in Response to Endoplasmic Reticulum Stress in Cancers. Cells. 2020;9(3).

2. Zaghdoudi S, Decaup E, Belhabib I, Samain R, Cassant-Sourdy S, Rochotte J, Brunel A, Schlaepfer D, Cros J, Neuzillet C, Strehaiano M, Alard A, Tomasini R, Rajeeve V, Perraud A, Mathonnet M, Pearce OM, Martineau Y, Pyronnet S, Bousquet C, Jean C. FAK activity in cancer-associated fibroblasts is a prognostic marker and a druggable key metastatic player in pancreatic cancer. EMBO Mol Med. 2020;12(11):e12010.

3. Larose H, et al. Whole Exome Sequencing reveals NOTCH1 mutations in anaplastic large cell lymphoma and points to Notch both as a key pathway and a potential therapeutic target. Haematologica. 2020 Apr 23.

4. Mussolin L, et al POBOTEIFCNL. Prognostic Factors in Childhood Anaplastic Large Cell Lymphoma: Long Term Results of the International ALCL99 Trial. Cancers (Basel). 2020;12(10):2747.

5. Congras A, Hoareau-Aveilla C, Caillet N, Tosolini M, Villarese P, Cieslak A, Rodriguez L, Asnafi V, Macintyre E, Egger G, Brousset P, Lamant L, Meggetto F. ALK-transformed mature T lymphocytes restore early thymus progenitor features. J Clin Invest. 2020;130(12):6395-408.

TEAM DOSE INDIVIDUALIZATION OF ANTICANCER DRUGS - DIAD

Team leader: Prof. Etienne Chatelut

Keywords: Population pharmacokinetics, platinum compounds, tyrosine kinase inhibitors, therapeutic drug monitoring, pharmacokinetic-pharmacodynamic relationships, PK-PD, pharmacogenetics, metabolism, radiolabeled molecules
Funding sources: PHRC, ANSM, ITMO Cancer
Research theme: The team carries out translational and clinical research to drive the dose individualization of anticancer drugs. Its work mostly involves identifying inter-individual variability in pharmacokinetics and pharmacogenetics that can be used to adapt treatments to each patient and thereby increase the efficacy of drug doses while reducing their toxicity.
Several studies applying the nonlinear mixed effects approach are being conducted in order to:
- Monitor the effects of drugs so that doses can be adjusted during a protocol,
- Determine how drugs are metabolized in order to assess their hepatotoxicity and potential side effects,
- Develop pharmacokinetic-pharmacodynamic modeling methods to quantify the effects of different treatments,
- Model pharmacokinetic and pharmacodynamic data for radiolabeled molecules.

MAJOR PUBLICATIONS IN 2020

1. Gallais F, Oberic L, Faguer S, Tavitian S, Lafont T, Marsili S, Brice A, Chatelut E, Puisset F. Body Surface Area Dosing of High-Dose Methotrexate Should be Reconsidered, Particularly in Overweight, Adult Patients. Ther Drug Monit. EPub 2020 Sep 10.
2. Gallais F, Ysebaert L, Despas F, De Barros S, Dupré L, Quillet-Mary A, Protin C, Thomas F, Obéric L, Allal B, Chatelut E, White-Koning M. Population Pharmacokinetics of Ibrutinib and Its Dihydrodiol Metabolite in Patients with Lymphoid Malignancies. Clin Pharmacokinet. 2020;59(9):1171-83.
3. Maillard M, Chevreau C, Le Louedec F, Cassou M, Delmas C, Gourdain L, Blay JY, Cupissol D, Bompas E, Italiano A, Isambert N, Delcambre-Lair C, Penel N, Bertucci F, Guillemet C, Plenecassagnes J, Foulon S, Chatelut É, Le Cesne A, Thomas F. Pharmacogenetic Study of Trabectedin-Induced Severe Hepatotoxicity in Patients with Advanced Soft Tissue Sarcoma. Cancers. 2020;12(12):E3647.
4. Moeung S, Chevreau C, Marsili S, Massart C, Fléchon A, Delva R, Gravis G, Lotz JP, Bay JO, Gross-Goupil M, Filleron T, Delmas C, Lafont T, Chatelut E, Thomas F. Pharmacokinetic and Pharmacogenetic Study of Etoposide in High-Dose Protocol (TI-CE) for Advanced Germ Cell Tumors. Pharm Res. 2020;37(7):147.
5. Puszkiel A, Arellano C, Vachoux C, Evrard A, Le Morvan V, Boyer JC, Robert J, Delmas C, Dalenc F, Debled M, Venat-Bouvet L, Jacot W, Dohollou N, Bernard-Marty C, Laharie-Mineur H, Filleron T, Roché H, Chatelut E, Thomas F, White-Koning M. Model-based Quantification of Impact of Genetic Polymorphisms and Co-Medications on Pharmacokinetics of Tamoxifen and Six Metabolites in Breast Cancer. Clin Pharmacol Ther. EPub 2020 Oct 12.

TEAM CHOLESTEROL METABOLISM AND THERAPEUTIC INNOVATIONS - CMATI

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leaders: Dr. Marc Poirot and Dr. Sandrine Silvente-Poirot

Keywords: Cholesterol, metabolism, oxysterols, dendrogenin, OCDO, tumor suppressor/promoter, autophagy, exosome, medicinal chemistry
Funding sources: ANR, INCa, Fondation Toulouse Cancer Santé, Ligue contre le cancer, IUCT-Oncopole, Institut Claudius Regaud
Research theme: The team's research into cholesterol metabolism dysregulation in cancers has revealed two new cholesterol derivatives that play a role in controlling oncogenesis. Although both molecules are derived from the same precursor, they have opposite effects. The first molecule, dendrogenin A (DDA), is a tumor suppressor that is present in healthy breast tissues but that disappears during carcinogenesis in favor of oncosterone, a tumor promoter. The team is thus currently characterizing this new metabolic branch of the cholesterol pathway in cancer. It is also studying the properties of these molecules in order to explore new therapies and to obtain a better understanding of the mechanisms underlying both acquired and intrinsic resistance to conventional treatments.
In 2020, the team showed that dendrogenin A, through its original anticancerous mechanism of action, was able to sensitize tumors to conventional chemotherapy. It laid the groundwork for exploring oncosterone biosynthesis as a new therapeutic target in cancer research.

MAJOR PUBLICATIONS IN 2020

1. Mouchel PL, Serhan N, Betous R, Farge T, Saland E, de Médina P, Hoffmann JS, Sarry JE, Poirot M, Silvente-Poirot S, Récher C. Dendrogenin A Enhances Anti-Leukemic Effect of Anthracycline in Acute Myeloid Leukemia. Cancers. 2020;12(10):2933.
2. de Médina P, Diallo K, Huc-Claustre E, Attia M, Soulès R, Silvente-Poirot S, Poirot M. The 5,6-epoxycholesterol metabolic pathway in breast cancer: Emergence of new pharmacological targets. Br J Pharmacol. 2020 Jul 21.
3. Serhan N, Mouchel PL, de Médina P, Segala G, Mougel A, Saland E, Rives A, Lamaziere A, Despres G, Sarry JE, Larrue C, Vergez F, Largeaud L, Record M, Récher C, Silvente-Poirot S, Poirot M. Dendrogenin A synergizes with Cytarabine to Kill Acute Myeloid Leukemia Cells In Vitro and In Vivo. Cancers. 2020;12(7):1725.
4. Shao W, et al. Cytoplasmic and Nuclear Forms of Thyroid Hormone Receptor β1 Are Inversely Associated with Survival in Primary Breast Cancer. Int J Mol Sci. 2020;21(1):330.
5. Martinez A, et al. Tumour and pelvic lymph node metabolic activity on FDG-PET/CT to stratify patients for para-aortic surgical staging in locally advanced cervical cancer. Eur J Nucl Med Mol Imaging. 2020;47(5):1252-60.

TEAM

OPTIMIZATION OF RADIOTHERAPY FROM MOLECULAR SIGNALING PATHWAYS TO CLINICAL TRIALS - RADOPT

Team leaders: Prof. Elizabeth Moyal and Dr. Christine Toulas

Keywords: Glioblastoma, radioresistance, heterogeneity, reprogramming, stem cells, transdifferentiation, FGFR, integrins, metabolic imaging, biomarkers, radioimmunotherapy

Funding sources: Aviesan, INCa, Inserm, ARC, Ligue contre le cancer, ARTC, Incyte, AstraZeneca, Bayer

Research theme: The team's objective is to optimize radiotherapy for patients with glioblastoma (GBM). To this end, it is exploring three research themes: intrinsic radioresistance, including the role of integrins and growth-factor signaling pathways; induced radioresistance via different GBM stem cell plasticity mechanisms, including transdifferentiation and reprogramming; and mechanisms involving DNA repair genes. Results of this research are translated into early phase clinical trials, designed and conducted by the IUCT-Oncopole's Radiotherapy Department, associated with studies of metabolic imaging biomarkers. New targets identified and confirmed, in partnership with pharmaceutical companies, are tested in clinical practice. The response profiles to these associations are studied in collaboration with the T2i team and other specialized imaging teams. The team coordinates several national and international projects: the MoGlimaging project (ITMO Cancer) studies the heterogeneity and modeling of resistance mechanisms in GBM; the SI2GMA project (SIGN'IT, Fondation ARC) aims at defining a multiparametric biological and imaging profile of therapeutic response to the combination of stereotactic radiotherapy and Durvalumab in patients included in the phase II STERIMGLI trial ; international collaboration (Worldwide Cancer UK) with Dr. Valiente (CNIO) to study the correlation between a tumor marker and the microenvironment of lung cancer brain metastases and their clinical radiosensitivity. In 2020, with the arrival of several physicists, the team has been restructured and is developing, in parallel, a new research axis dedicated to multimodal image analysis and dose delivery modeling.

MAJOR PUBLICATIONS IN 2020

1. Bertorello J, Sesen J, Gilhodes J, Evrard S, Courtade-Saïdi M, Augustus M, Uro-Coste E, Toulas C, Moyal EC-J, Seva C, Dassi E, Cammas A, Skuli N, Millevoi S. Translation reprogramming by eIF3 linked to glioblastoma resistance. NAR Cancer. 2020; 2(3).

2. Dalmasso C, Pagès C, Chaltiel L, Brun A, Sibaud V, Boulinguez S, Chira C, Moyal E, Lubrano V, Meyer N, Modesto A. Survival estimation of melanoma patients with brain metastasis using the Melanoma-molGPA score: external validation from a French cohort. Melanoma Res. 2020; 30(5):472–6.

3. Gouazé-Andersson V, Cohen-Jonathan Moyal E. New Avenues in Radiotherapy of Glioblastoma: from Bench to Bedside. Curr Treat Options Neurol. 2020; 22, 45.

4. Kowalski-Chauvel A, Lacore MG, Arnauduc F, Delmas C, Toulas C, Cohen-Jonathan-Moyal E, Seva C. The m6A RNA Demethylase ALKBH5 Promotes Radioresistance and Invasion Capability of Glioma Stem Cells. Cancers. 2020;13(1):E40.

5. Barbeiro AR, Parent L, Vieillevigne L, Ferrand R, Franceries X. Dosimetric performance of continuous EPID imaging in stereotactic treatment conditions. Phys Med. 2020; 78, 117–22.

TEAM

THERAPEUTIC INNOVATION IN PANCREATIC CANCER - ImPACT

Team leader: Dr. Pierre Cordelier

Keywords: Gene therapy, pancreatic cancer, oncolytic virus, mechanisms of oncogenesis and of therapeutic resistance

Funding sources: Fondation ARC, Ligue Nationale contre le cancer, ImCore Roche Genentech, Occitanie Region

Research theme: The team's goal is to better understand molecular bases underlying pancreatic oncogenesis and therapeutic resistance in order to develop innovative treatments, particularly gene therapy, to improve patient care. In 2020, the team's clinicians, founders of the Clinicoanatomic database for adenocarcinoma (BACAP), contributed to highlighting a new prognostic molecular gradient predicting clinical outcome (1). From a basic research perspective, the team furthered its demonstration of the role played by TRIP12, a protein overexpressed in pancreatic cancer, in the cell cycle and chromosomic stability (2). Finally, the team published an overview in a very high-impact journal on the role of KRAS in diagnosis, prognosis and treatment of pancreatic cancer (3), as well as two literature reviews on TRIP12 (4) and cytidine deaminase, an emerging target of interest in this cancer (5).

MAJOR PUBLICATIONS IN 2020

1. Nicolle R, Blum Y, Duconseil P, Vanbrugghe C, Brandone N, Poizat F, Roques J, Bigonnet M, Gayet O, Rubis M, Elarouci N, Armenoult L, Ayadi M, de Reyniès A, Giovannini M, Grandval P, Garcia S, Canivet C, Cros J, Bournet B, Buscail L; BACAP Consortium, Moutardier V, Gilabert M, Iovanna J, Dusetti N. Establishment of a pancreatic adenocarcinoma molecular gradient (PAMG) that predicts the clinical outcome of pancreatic cancer. EBioMedicine. 2020 Jul;57:102858.

2. Larrieu D, Brunet M, Vargas C, Hanoun N, Ligat L, Dagnon L, Lulka H, Pommier RM, Selves J, Jády BE, Bartholin L, Cordelier P, Dufresne M, Torrisani J. The E3 ubiquitin ligase TRIP12 participates in cell cycle progression and chromosome stability. Sci Rep. 2020 Jan 21;10(1):789.

3. Buscail L, Bournet B, Cordelier P. Role of oncogenic KRAS in the diagnosis, prognosis and treatment of pancreatic cancer. Nat Rev Gastroenterol Hepatol. 2020 Mar;17(3):153-68.

4. Brunet M, Vargas C, Larrieu D, Torrisani J, Dufresne M. E3 Ubiquitin Ligase TRIP12: Regulation, Structure, and Physiopathological Functions. Int J Mol Sci. 2020 Nov 12;21(22):8515.

5. Frances A, Cordelier P. The Emerging Role of Cytidine Deaminase in Human Diseases: A New Opportunity for Therapy? Mol Ther. 2020 Feb 5;28(2):357-66.

TEAM ONCOGENOMICS AND IMMUNOLOGY OF MULTIPLE MYELOMA - GENIM

TEAM ACCREDITED BY THE FONDATION ARC POUR LA RECHERCHE SUR LE CANCER

Team leaders: Prof. Hervé Avet-Loiseau and Dr. Ludovic Martinet

Keywords: Multiple myeloma, pharmacogenomics, immunology, microenvironment, NGS
Funding sources: INCa, Fondation ARC pour la Recherche sur le Cancer, Ligue contre le cancer, Cancer Research Institute, Cancéropôle GSO
Research theme: The team is completely devoted to understanding and targeting multiple myeloma (MM), a devastating hematological cancer accounting for 5,000 new cases per year in France. More specifically, the team studies intrinsic (genomic) and extrinsic (immune) factors having an impact on the development of myeloma and the response to treatment. The first objective is to develop translational research on genomic alterations in tumors and molecular heterogeneity, to better understand the mechanisms underlying the aggressiveness and resistance of MM and thereby translate this work into patient care. The second objective is to understand the immune parameters limiting or contributing to MM development in order to propose new immunotherapeutic approaches.

MAJOR PUBLICATIONS IN 2020

1. Weulersse M, Asrir A, Pichler AC, Lemaitre L, Braun M, Carrié N, Joubert MV, Le Moine M, Do Souto L, Gaud G, Das I, Brauns E, Scarlata CM, Morandi E, Sundarrajan A, Cuisinier M, Buisson L, Maheo S, Kassem S, Agesta A, Pérès M, Verhoeyen E, Martinez A, Mazieres J, Dupré L, Gossye T, Pancaldi V, Guillerey C, Ayyoub M, Dejean AS, Saoudi A, Goriely S, Avet-Loiseau H, Bald T, Smyth MJ, Martinet L. Eomes-Dependent Loss of the Co-activating Receptor CD226 Restrains CD8+ T Cell Anti-tumor Functions and Limits the Efficacy of Cancer Immunotherapy. Immunity. 2020;53(4):824-39.
2. Braun M, Aguilera AR, Sundarrajan A, Corvino D, Stannard K, Krumeich S, Das I, Lima LG, Meza Guzman LG, Li K, Li R, Salim N, Jorge MV, Ham S, Kelly G, Vari F, Lepletier A, Raghavendra A, Pearson S, Madore J, Jacquelin S, Effern M, Quine B, Koufariotis LT, Casey M, Nakamura K, Seo EY, Hölzel M, Geyer M, Kristiansen G, Taheri T, Ahern E, Hughes BGM, Wilmott JS, Long GV, Scolyer RA, Batstone MD, Landsberg J, Dietrich D, Pop OT, Flatz L, Dougall WC, Veillette A, Nicholson SE, Möller A, Johnston RJ, Martinet L, Smyth MJ, Bald T. CD155 on Tumor Cells Drives Resistance to Immunotherapy by Inducing the Degradation of the Activating Receptor CD226 in CD8+ T Cells. Immunity. 2020;53(4):805-23.
3. Chari A, Samur MK, Martinez-Lopez J, Cook G, Biran N, Yong KL, Hungria VTM, Engelhardt M, Gay F, Garcia-Feria A, Oliva S, Oostvogels R, Gozzetti A, Rosenbaum CA, Kumar SK, Stadtmauer E, Einsele H, Beksac M, Weisel KC, Anderson KC, Mateos MV, Moreau P, San Miguel J, Munshi NC, Avet-Loiseau H. Clinical Features Associated with COVID-19 Outcome in MM: First Results from International Myeloma Society Dataset. Blood. EPub 2020 Nov 6.
4. Samur MK, Aktas Samur A, Fulciniti M, Szalat R, Han T, Shammas M, Richardson P, Magrangeas F, Minvielle S, Corre J, Moreau P, Thakurta A, Anderson KC, Parmigiani G, Avet-Loiseau H, Munshi NC. Genome-Wide Somatic Alterations in Multiple Myeloma Reveal a Superior Outcome Group. J Clin Oncol. 2020;38(27):3107-18.
5. Corre J, Montes L, Martin E, Perrot A, Caillot D, Leleu X, Belhadj K, Facon T, Hulin C, Mohty M, Fontan J, Macro M, Brechignac S, Jaccard A, Stoppa AM, Orsini-Piocelle F, Adiko D, Voillat L, Keddar F, Barry M, Demarquette H, Certain MN, Plantier I, Roussel M, Hébraud B, Filleron T, Attal M, Avet-Loiseau H. Early relapse after autologous transplant for myeloma is associated with poor survival regardless of cytogenetic risk. Haematologica. 2020;105(9):e480-3.

TEAM NEW IMMUNOTHERAPIES AGAINST LYMPHOMAS - NoLymIT

Team leader: Prof. Camille Laurent

Keywords: Lymphoma, 3D model, single cell RNAseq and bioinformatic tools, γδ T cells, post-transcriptional regulation of immune checkpoints
Funding sources: LabEx TOUCAN, Ligue contre le cancer, Fondation ARC, Fondation Toulouse Cancer Santé, POCTEFA, imCore Roche
Research theme: The team's research involves the innate and adaptive immune response in lymphoma, with a special mention of work on γδ T cells and the regulation mechanisms of immune checkpoints (1, 2). The team recently introduced Single Cell RNAseq techniques and developed bioinformatic tools to explore the functional status and the maturation/differentiation stage of cytotoxic effectors at single cell level in lymph node or blood samples from lymphoma patients (3). Privileged access to different cohorts of patients with lymphoma also enabled to identify response biomarkers (4) and to implement a screening platform in 3D models from samples of lymphoma patients.

MAJOR PUBLICATIONS IN 2020

1. Laplagne C, Meddour S, Figarol S, Michelas M, Calvayrac O, Favre G, Laurent C, Fournié JJ, Cabantous S, Poupot M. Vγ9Vδ2 T Cells Activation Through Phosphoantigens Can Be Impaired by a RHOB Rerouting in Lung Cancer. Front Immunol. 2020;11:1396.
2. Curdy N, Lanvin O, Cadot S, Laurent C, Fournié JJ, Franchini DM. Stress Granules in the Post-transcriptional Regulation of Immune Cells. Front Cell Dev Biol. 2021 Jan 14;8:611185.
3. Pont F, Tosolini M, Gao O, Perrier M, Madrid-Mencia M, Huang TS, Neuvial P, Ayyoub M, Nazor K, Fournié JJ. Single-Cell Virtual Cytometer allows user-friendly and versatile analysis and visualization of multimodal single cell RNAseq datasets. NAR Genom Bioinform. 2020;2(2).
4. Cadot S, Valle C, Tosolini M, Pont F, Largeaud L, Laurent C, Fournie JJ, Ysebaert L, Quillet-Mary A. Longitudinal CITE-Seq profiling of chronic lymphocytic leukemia during ibrutinib treatment: evolution of leukemic and immune cells at relapse. Biomark Res. 2020;8(1):72.
5. Rossi C, Tosolini M, Gravelle P, Pericart S, Kanoun S, Evrard S, Gilhodes J, Franchini DM, Amara N, Syrykh C, Bories P, Oberic L, Ysebaert L, Martin L, Ramla S, Robert P, Tabouret-Viaud C, Casasnovas RO, Fournié JJ, Bezombes C, Laurent C. Baseline SUVmax is related to tumor cell proliferation and patient outcome in follicular lymphoma. Haematologica. 2020 Dec 17;

TEAM ALTERATION OF TRANSCRIPTION FACTORS IN ACUTE LEUKEMIAS - ALTFAL

Team leader: Prof. Eric Delabesse

Keywords: Acute leukemia, genetic alterations, predispositions
Funding sources: Institut Carnot OPALE, ANR, INCa, Ligue contre le cancer, Fondation ARC, Occitanie Region, Association Les 111 des Arts, Société Française des cancers de l'enfant, Association Capucine, Association Laurette Fugain, Association Cassandra, Association Constance la petite guerrière astronaute
Research theme: Hematopoiesis is the process by which all blood cells are obtained from a hematopoietic stem cell (SC) in defined proportions. During this process, which takes place mainly in bone marrow, stem cells differentiate into (mature) functional cells. Deregulation of hematopoiesis can lead to acute leukemia (AL), in which the blockage of stem cell differentiation leads to uncontrolled proliferation of immature cells that flood the marrow and then the blood. The team's work, lying at the interface between clinical and basic research, explores mutations both acquired during a person's lifetime and inherited. It seeks to identify genomic alterations in the factors controlling hematopoiesis in AL patients and to model these alterations in cell culture and mouse models. Recently, the team identified mutations in transcription factors (PAX5, GATA2 and USP7) and recreated them in mice. These models make it possible to better understand the impact of these mutations on normal blood production and on initiation, transformation and relapse of leukemia. They also make it possible to test innovative therapies targeting such mutations. In 2020, the team received the scientific award of the French Society of Hematology (SFH) for its work analyzing the mouse model in Gata2 germinal mutation.

MAJOR PUBLICATIONS IN 2020

1. Laurent AP, Siret A, Ignacimouttou C, Panchal K, Diop M, Jenni S, Tsai YC, Roos-Weil D, Aid Z, Prade N, Lagarde S, Plassard D, Pierron G, Daudigeos E, Lecluse Y, Droin N, Bornhauser BC, Cheung LC, Crispino JD, Gaudry M, Bernard OA, Macintyre E, Barin Bonnigal C, Kotecha RS, Geoerger B, Ballerini P, Bourquin JP, Delabesse E, Mercher T, Malinge S. Constitutive activation of RAS/MAPK pathway cooperates with trisomy 21 and is therapeutically exploitable in Down syndrome B-cell leukemia. Clin Cancer Res. 2020;26(13):3307-18.

2. Largeaud L, Cornillet-Lefebvre P, Hamel JF, Dumas PY, Prade N, Dufrechou S, Plenecassagnes J, Luquet I, Blanchet O, Banos A, Béné MC, Bernard M, Bertoli S, Bonmati C, Fornecker LM, Guièze R, Haddaoui L, Hunault M, Ianotto JC, Jourdan E, Ojeda M, Peterlin P, Vey N, Zerazhi H, Yosr H, Mineur A, Cahn JY, Ifrah N, Récher C, Pigneux A, Delabesse E; French Innovative Leukemia Organization (FILO). Lomustine is beneficial to older AML with ELN2017 adverse risk profile and intermediate karyotype: a FILO study. Leukemia. 2020 Sep 18.

3. Largeaud L, Bertoli S, Berard E, Dufrechou S, Prade N, et al. Outcome of relapsed/refractory AML patients with IDH1(R132) mutations in real life before the era of IDH1 inhibitors. Leuk Lymphoma. 2020;61(2):473-6.

4. Fagnan A, et al. Human erythroleukemia genetics and transcriptomes identify master transcription factors as functional disease drivers. Blood. 2020;136(6):698-714.

5. Bories P, Prade N, Lagarde S, Cabarrou B, Largeaud L, et al. Impact of TP53 mutations in acute myeloid leukemia patients treated with azacitidine. PLoS One. 2020;15(10):e0238795.

TEAM INTEGRATING CELL SIGNALING AND CLASS I, II, III PI3K - SigDYN

Team leader: Dr. Julie Guillermet-Guibert

Keywords: oncogenic signaling, genetically modified mice, targeted therapies, mechanobiology, bio-impression
Funding sources: ANR Jeune Chercheuse, Occitanie Region/FEDER, Plan Cancer PCSI, Fondation Toulouse Cancer Santé, Fondation de France
Research theme: The team focuses on the most frequent oncogenic signaling pathway, PI3K. Indeed. PI3Ks are found, overactivated in cancer cells, but also in cells of the tumor microenvironment —immune cells, fibroblasts, non-transformed cells. The aim is to define the external chemical or mechanical signals associated with tumors and to understand how class I, II and III PI3Ks integrate these signals to foster tumor progression, so as to propose and validate new (targeted) therapies in pancreatic adenocarcinoma (PAC) and high-grade ovarian carcinomas. In 2020, the team showed how compressing a tumor organoid prevented cellular proliferation. Since chemotherapies target cells involved in the cell cycle, compressing tumor cells growing in a constrained space might thus be responsible for chemotherapy resistance, particularly for PAC. Bioprinting approaches have made it possible to reconstruct the tissue niche from where PAC originates to thus better understand the key points of this biological process. Finally, two patents have been internationally validated for a new PAC therapeutic strategy and a companion molecular marker.

MAJOR PUBLICATIONS IN 2020

1. Rizzuti IF, Mascheroni P, Arcucci S, Ben-Mériem Z, Prunet A, Barentin C, Rivière C, Delanoë-Ayari H, Hatzikirou H, Guillermet-Guibert J*, Delarue M*. Mechanical Control of Cell Proliferation Increases Resistance to Chemotherapeutic Agents. Phys Rev Lett. 2020 Sep 18;125(12):128103.

2. Hakobyan D, Médina C, Dusserre N, Stachowicz ML, Handschin C, Fricain JC, Guillermet-Guibert J*, Oliveira H*. Laser-assisted 3D bioprinting of exocrine pancreas spheroid models for cancer initiation study. Biofabrication. 2020 Apr 16;12(3):035001.

3. Brevet : Nouveau marqueur permettant de prédire la sensibilité à des inhibiteurs de PI3K. Guillermet-Guibert J, Douche T, Mouton-Barbosa E, Schiltz O, Bousquet MP, Cintas C. EP3713963 A1 ; Publication: 2020-09-30

4. Brevet : Polythérapie du cancer du pancréas. Guillermet-Guibert J, Reichert M, Cintas C. EP3694511 A1 ; Publication : 2020-08-19

TEAM

METABOLISM AND THERAPEUTIC RESISTANCE IN ACUTE MYELOID LEUKEMIA (AML) - METAML

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER, LABEX TOUCAN2.0, INSTITUT CARNOT OPALE

Team leader: Dr. Jean-Emmanuel Sarry

Keywords: Leukemia, drug resistance, mitochondria, oncometabolism, autophagy, RNA

Funding sources: Ligue Nationale et Régionale de Lutte Contre le Cancer, LabEx TOUCAN, Fondation Toulouse Cancer Santé, GILEAD Hemato-Oncology, Fondation ARC, H2020-MSCA-IF-GF-2019, Occitanie Region, Interreg POCTEFA

Research theme: The team's goal is to understand and target the metabolic and mitochondrial mechanisms responsible for therapeutic resistance in acute myeloid leukemia (AML). Therapeutic resistance is the major reason explaining recurrences of AML and patients' poor prognosis. The team has shown that this resistance is initiated by cells whose mitochondria have a very high level of oxidative and energetic activity ("OxPHOS") following conventional chemotherapy, but also after recently available targeted therapies. This phenotype results from the induction of a transcriptional program in response to mitochondrial stress that regulates mitochondrial homeostasis, redox and energy metabolism. These studies have led to several patent applications concerning new molecular targets (for ex. CD39, CALCRL, ADM) whose inhibition sensitizes resistant cells to chemotherapy. The team is also currently working on the role of transcriptional regulation and of RNA splicing, as well as on leukemic and host autophagy, a catabolic process involved in cell metabolism regulation, in mitochondrial adaptation and in the metabolic heterogeneity of resistant cells in AML.

MAJOR PUBLICATIONS IN 2020

1. Stuani L, Sarry JE. Microenvironmental aspartate preserves leukemic cells from chemotherapeutics-induced metabolic collapse. Cell Metab. 2020;32, 321-3.

2. Bosc C*, Broin N*, Fanjul M, Saland E, Farge T, Courdy C, Batut A, Masoud R, Larrue C, Scotland S, Skuli S, Espagnolle N, Pagès JC, Carrier A, Bost F, Bertrand-Michel J, Tamburini J, Récher C, Bertoli S, Mansat-De Mas V, Manenti S, Sarry JE*, Joffre C*. Autophagy regulates fatty acid availability for oxidative phosphorylation through mitochondria-endoplasmic reticulum contact sites. Nat Commun. 2020;11(1):4056.

3. Aroua N, Boet E, Ghisi M, Nicolau-Travers ML, Saland E, Gwilliam R, de Toni F, Hosseini M, Mouchel PL, Farge T, Bosc C, Stuani L, Sabatier M, Mazed F, Larrue C, Jarrou L, Gandarillas S, Bardotti M, Picard M, Synykh C, Laurent C, Gotanegre M, Bonnefoy N, Bellvert F, Portais JC, Nicot N, Azuaje F, Kaoma T, Joffre C, Tamburini J, Recher C, Vergez F, Sarry JE. Extracellular ATP and CD39 activate cAMP-mediated mitochondrial stress response to promote cytarabine resistance in acute myeloid leukemia. Cancer Discov. 2020;10(10):1544-65.

TEAM

ONCOGENESIS OF SARCOMAS - ONCOSARC

Team leader: Dr. Frédéric Chibon

Keywords: Oncogenesis, sarcomas, genome, metastasis, hybrid cells

Funding sources: INCa (PRTK), PHRC

Research theme: The team's research focuses on the chromosomal mechanisms underlying the oncogenesis of pleomorphic sarcomas, which are characterized by high chromosomal instability. Although this work has identified some important genes in this oncogenesis (MDM2, CDK4, TP53, RB1, MYOCD1) and linked the tumors' aggressiveness to this chromosomal instability, its main drivers remain unclear. The team is now focusing on two main themes: oncogenesis at the single cell and spatial level, and cellular mechanisms, in particular, cell fusion, previously observed by the team, that leads to significant remodeling of cell metabolism and tumor genome, producing hybrids mimicking the disease as seen in patients. The team is also developing tools to improve diagnosis and monitor the clinical evolution of patients. Having previously identified an almost universal expression signature in sarcomas, the team, through technology transfer, has been working on transforming this signature into practical patient care. Clinical trials based on the application of this signature are underway. The first inclusions were made in 2020 for one of these trials, promoted by the IUCT-Oncopole. This phase 3 clinical trial, CHIC—STS, will allow the team to test not only the value of the CINSARC signature in detecting patients potentially benefitting from systemic therapy, but more globally, of those benefitting from chemotherapy. Furthermore, the team has filed a European patent application to protect a new prognostic marker based on measuring chromosomic instability associated with replication and transcription.

MAJOR PUBLICATIONS IN 2020

1. Merle C, Thébault N, LeGuellec S, Baud J, Pérot G, Lesluyes T, Delespaul L, Lartigue L, Chibon F. Tetraploidization of Immortalized Myoblasts Induced by Cell Fusion Drives Myogenic Sarcoma Development with DMD Deletion. Cancers. 2020;12(5):E1281.

2. Lesluyes T, Chibon F. A global and integrated analysis of CINSARC-associated genetic defects. Cancer Res. 2020 Oct 6.

3. Lartigue L, Merle C, Lagarde P, Delespaul L, Lesluyes T, Le Guellec S, Pérot G, Leroy L, Coindre JM, Chibon F. Genome remodeling upon mesenchymal tumor cell fusion contributes to tumor progression and metastatic spread. Oncogene. 2020;39(21):4198-211.

4. Croce S, Lesluyes T, Valle C, M'Hamdi L, Thébault N, Pérot G, Stoeckle E, Noël JC, Fontanges Q, Devouassoux-Shisheboran M, Ouerleu D, Guyon F, Floquet A, Chakiba C, Mayeur L, Rebier F, MacGrogan GM, Soubeyran I, Le Guellec S, Chibon F. The Nanocind Signature Is an Independent Prognosticator of Recurrence and Death in Uterine Leiomyosarcomas. Clin Cancer Res. 2020;26(4):855-61.

TEAM MOLECULAR DYNAMICS OF LYMPHOCYTE INTERACTIONS - DynAct

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leader: Dr. Salvatore Valitutti

Keywords: Immunological synapse, cytotoxic T-cells, supramolecular attack particles (SMAP), tumor immunology, cell-mediated cytotoxicity, live-cell imaging

Funding sources: Ligue contre le cancer, ANR - LabEx TOUCAN, Occitanie Region, Fondation Toulouse Cancer Santé, F. Hoffmann-La Roche, Bristol-Myers Squibb

Research theme: The five major lines of research pursued by the team in 2020 involved: i) investigating why the ability of human cytotoxic T-cells (CTCs) to kill target tumor cells varies (1); ii) more clearly elucidating the molecular mechanisms of CTCs delivering fatal blows (2) ; iii) studying ex vivo the phenotype and function of CTCs in patients' tissues; iv) determining the molecular mechanisms that allow aggressive tumors such as melanomas to resist attacks by CTCs at the lytic synapse level; and v) developing mathematical models to mimic the interactions between CTCs and target tumor cells. The team strengthened its capabilities by recruiting a post-doctoral researcher to work with its own computer scientists and those from the IRIT. Their aim is to model the competitive CTC/tumor cell interaction to define the best scenarios to shift the balance between CTC efficacy and tumor cell resistance in favor of CTCs. One of the team's achievements was being awarded a prestigious ERC Synergy grant for the ATTACK project to collaborate with British, German and Italian colleagues on SMAPs and their use in cancer therapy.

MAJOR PUBLICATIONS IN 2020

1.Balint Š, Müller S, Fischer R, Kessler BM, Harkiolaki M, Valitutti S, Dustin ML. Supramolecular attack particles are autonomous killing entities released from cytotoxic T cells. Science. EPub 2020 May 7.

2. Biolato AM, Filali L, Wurzer H, Hoffmann C, Gargiulo E, Valitutti S, Thomas C. Actin remodeling and vesicular trafficking at the tumor cell side of the immunological synapse direct evasion from cytotoxic lymphocytes. Int Rev Cell Mol Biol. 2020;356:99-130.

3. Lafouresse F, Jugele R, Müller S, Doineau M, Duplan-Eche V, Espinosa E, Puisségur MP, Gadat S, Valitutti S. Stochastic asymmetric repartition of lytic machinery in dividing human CD8 + T cells generates heterogeneous killing behavior. eLife. EPub 2021;

TEAM NETWORK BIOLOGY MODELING FOR ONCOIMMUNOLOGY - NetB(IO)²

TEAM ACCREDITED BY THE CHAIRE PIERRE FABRE - FONDATION TOULOUSE CANCER SANTÉ - INSERM (CRCT)

Team leader: Dr. Vera Pancaldi

Keywords: Machine learning, network theory, chromatin architecture, mathematical models, heterogeneity, cancer, oncoimmunology,

Funding sources: Chaire Pierre Fabre - Fondation Toulouse Cancer Santé – Inserm, Jansssen Horizon AI

Research theme: The team applies bioinformatics methods to oncoimmunology to study the impact of the variability in patient profiles (transcriptome and immune cell characteristics) on responses to treatment, integrating multi-omics data, and on single cells, via machine learning methods. The team is at the heart of collaboration between the CRCT, the Toulouse University Hospital and Pierre Fabre to collect and analyze multidimensional data from lung cancer patients to personalize their treatment and optimize immunotherapy (LungPredict). The long-term objective is to characterize interactions between different cell types in the tumor microenvironment, using "agent-based" and Boolean models to work towards simulations of the tumor microenvironment.

Using innovative methods of network theory, the team is also exploring linking immune cell variability and plasticity to their epigenome. Tools for constructing and analyzing chromatin interaction networks have also been developed to study the variations in the epigenome of immune cells in healthy donors and patients (GARDEN-NET) (2). The team participated in the creation of databases on the effect of Covid19 on lung cancer patients (TERAVOLT International Consortium). With Italian colleagues, the team used network medicine approaches to search for drug candidates and study the systemic nature of the disease (CovMulNet19 https://covmulnet19.fbk.eu/) (4). The team also proposed a method for revealing the molecular bases of comorbidities between different diseases (5).

MAJOR PUBLICATIONS IN 2020

1. Marku M, Verstraete N, Raynal F, Madrid-Mencía M, Domagala M, Fournié JJ, Ysebaert L, Poupot M, Pancaldi V. Insights on TAM Formation from a Boolean Model of Macrophage Polarization Based on In Vitro Studies. Cancers. 2020. 12(12) :3664.

2. Madrid-Mencía M, Raineri E, Cao TBN, Pancaldi V. Using GARDEN-NET and ChAseR to explore human haematopoietic 3D chromatin interaction networks. Nucleic Acids Res. 2020;48(8):4066-80.

3. Garassino MC et al ; TERAVOLT investigators. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol. 2020; 21 (7) ; 914-22..

4. Verstraete, N., Jurman, G., Bertagnolli, G., Ghavasieh, A., Pancaldi, V., De Domenico, M., 2020. CovMulNet19, Integrating Proteins, Diseases, Drugs, and Symptoms: A Network Medicine Approach to COVID-19. Netw Syst Med. 2020;3(1):130-41.

5. Sánchez-Valle J, Tejero H, Fernández JM, Juan D, Urda-García B, Capella-Gutiérrez S, Al-Shahrour F, Tabarés-Seisdedos R, Baudot A, Pancaldi V, Valencia A. Interpreting molecular similarity between patients as a determinant of disease comorbidity relationships. Nat Commun. 2020;11(1):2854.

TECHNOLOGY CLUSTER

Manager: Dr. Frédéric Lopez

The Technology Cluster (TC) provides cutting-edge skills, expertise and technologies to support the research activities of the CRCT's and IUCT-Oncopole's research teams. Its engineers help researchers design projects and experiments, provide training on how to use open-access equipment, advise on interpreting and presenting research findings, and assist with writing papers and valorizing results. The Technology Cluster has both ISO 9001-2015 and NFX 50-900 certification.

Technological focus

In collaboration with Dr. J-J. Fournié, the TC is developing the first "spatial Transcriptomic" project making it possible to map gene expression at the level of a single cell (Single cell RNA Seq), all the while maintaining the spatial arrangement of cells within a given tissue. The CRCT used the method for the first time in September 2020, relying on 10x Genomics technology. A frozen tissue slice is placed on a slide covered with probes to capture poly-d(T) specifically barcoded according to their position on the slide. Following hematoxylin and eosin staining and imaging, the tissue is lysed to allow mRNA to diffuse towards adjacent capture probes. A NGS library is obtained from the captured mRNA. Thanks to positioning barcodes, molecular information is superimposed on the morphological image of the tissue and replaced in the tissue environment. This technology implies close collaboration between the team and the histologic, genomic-transcriptomic, imaging and bioinformatic platforms.

New equipment in 2020

- Clariostar upgrade for HTRF (Homogeneous Time-Resolved Fluorescence)
- Imaris software: image analysis, 3D/4D reconstruction
- 384-well qPCR system: QuantStudio (QS5)
- QuBit system for fluorimetric dosing of nucleic acids

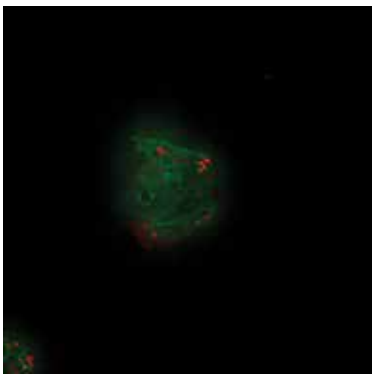
>>> https://www.poletechno-crct.inserm.fr/

MAJOR PUBLICATIONS IN 2020

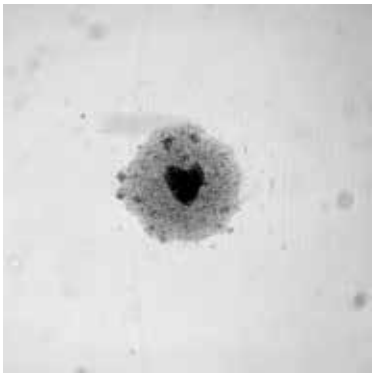
In 2020, the Technology Cluster's work was highlighted in 14 publications, one of which presented the conception of a new software tool:

Pont F, Tosolini M, Gao O, Perrier M, Madrid-Mencía M, Huang TS, Neuvial P, Ayoub M, Nazor K, Fournié JJ. Single-Cell Virtual Cytometer allows user-friendly and versatile analysis and visualization of multimodal single cell RNAseq datasets. NAR Genom Bioinform. 2020 Apr 20;2(2):lqaa025.

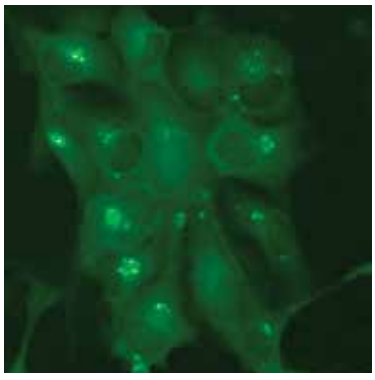
Three photos taken on the Operetta Imaging platform selected for the PerkinElmer 2021 calendar



Pancreatic cancer organoid after Cytokeratine 19 and Ki67 immunostaining. Photo: Marjorie Fanjul (MICROPANC) and Laetitia Ligat (Cellular Imaging, TC).



Spheroid formed from patient lymphoma cells. Photo: Christine Bezombes, Fabien Gava and Carla Faria (NoLymT).



Primary pancreatic cancer cells infected by an oncolytic virus. Photo: Agathe Redouté (ImPACT) and Laetitia Ligat (Cellular Imaging, TC).

Interconnections CRCT – IUCT-O

Because translating research findings into clinical and therapeutic applications is a key component of the Oncopole concept, the campus was designed so the CRCT would be adjacent to the IUCT-Oncopole. This proximity has led to parallel increases in the number of clinicians affiliated to the CRCT's research teams and the number of researchers who contribute to the IUCT-Oncopole's organ coordination committees.
The four projects below, winners of the 2020 Translational@IUCT-O call for proposals, co-sponsored by the Fondation Toulouse Cancer Santé, exemplify the dynamics that have been built up on the site.

CLUSTER

The malignant cell aggregate in serous fluid: a mechanism of tumor progression?
Dr. Céline Basset (Pathology Department, IUCT-Oncopole) and Dr. Julie Guillermet-Guibert (CRCT team SigDYN)
The project aims first to develop and automate a new technique for analyzing general characteristics of serous effusions, such as cell aggregates, in addition to those routinely used, to identify prognostic morphological characteristics to then, in turn, improve diagnosis and understand their molecular determinants to propose new therapies. Indeed, metastatic cancer commonly shows up as a serous effusion, resulting from an accumulation of fluid in the pleural, pericardial and peritoneal cavities. Microscopic examination on cytospin rapidly gives an indication of the malignity and the histological type according to cell morphology. The final diagnosis can be confirmed by immunochemistry on cytospin that also provides a specific etiology. Nevertheless, the use of these techniques to improve molecular therapeutic or prognostic targeting still remains limited.

Comm'in BC

Correlation between the aggressiveness of ER+ breast cancer and the functional profile of CD8+ T cells infiltrating patients' tissues and antigen-presenting cells?
Dr. Salvatore Valitutti (CRCT team DynAct) and Dr. Camille Franchet (Pathology Department) - Partnership with the IUCT-Oncopole Methodology Department
Few studies have focused on the role of the tumor immune microenvironment in breast cancer. Tissue-resident memory T cells (TRM) have recently appeared to be a potential target in onco-immunology, due to their high cytotoxic capabilities. Moreover, certain antigen-presenting cells (APC) are seen to play a positive role in anti-tumor immune response. The Comm'in BC project is based on the hypothesis of a functional interaction of certain APCs with TRMs in the tumor microenvironment, since certain APCs are capable of either stimulating or inhibiting TRM function, and both APC sub-types themselves compete with each other. The aim is to obtain "functional mapping" of TRMs and APCs in the ER+ breast cancer microenvironment (combining classic immuno-histological techniques and latest-generation confocal microscopy) to determine whether activation/interaction of these cells is modified in the tumor and correlated with disease aggressiveness.

GAMER

Identifying genomic abnormalities in myeloma by targeted sequencing in patients presenting an unexplained early relapse.

Dr. Jill Corre (CRCT team GENIM) and Dr. Aurore Perrot (OCC Hematology, IUCT-Oncopole)

Myeloma is a pathology with significant genomic heterogeneity and very few recurring mutations. Little research has thus been developed to date to study the prognostic impact of mutations. Since the IUCT-Oncopole Myeloma Genomics team centralizes a large proportion of the myeloma analyses performed in France, it is able to launch large-scale genomic studies.

The current definition of cytogenetic risk in multiple myeloma, based solely on two or three markers of poor prognosis, seems both restrictive and too simplistic. The prognostic impact of oncogenetic mutations must be elucidated, but such a study requires a large cohort of patients, given the rarity of recurrence. The GAMER project is thus based on the assumption that exploring genomic data of newly diagnosed patients presenting an early relapse (ER) after intensive treatment will help specifically identify patients at high-risk. Furthermore, genomic analysis of paired samples (diagnosis vs ER) will make it possible to better understand the molecular mechanisms leading to rapid relapse. This project hinges on the targeted next-generation sequencing (NGS) of malignant plasmocytes selected from 220 patients at diagnosis and 30 patients at both diagnosis and relapse.

DEMETAR

Deciphering mechanisms of resistance to targeted therapies in CLL.

Prof. Loïc Ysebaert (OCC Hematology, IUCT-Oncopole) and Dr. Anne Quillet-Mary (CRCT team NoLymIT)

This project seeks to identify new therapeutic targets for patients with chronic lymphocytic leukemia (CLL) who are resistant to current targeted therapies. It is based on the observation that only 60% of these patients develop mutations following treatment. Practically speaking, from blood samples of patients treated with ibrutinib, tumor cell transcriptomic and protein profiles and their environment will be studied at the level of the single cell (CITEseq technique). "Cell maps" will thus be generated in order to identify possible "transcriptomic profiles", allowing to differentiate classic progressive forms from Richter syndromes corresponding to aggressive variations of the disease. Currently, however, these aggressive forms can only be identified by anatomopathologic analyses. The objective is first to understand the resistance mechanisms to ibrutinib (independent of mutations), to then identify the different signaling pathways between the two entities (progression vs Richter), and finally to pinpoint new therapeutic targets that can be validated in vitro.

Finally, in 2020, the IUCT Public Interest Group (GIP) and the Toulouse Cancer Santé Foundation (FTCS) launched the 10th call for joint projects on the theme of "Initial mechanisms of oncogenesis and early diagnosis of cancer". The Scientific Council received and evaluated seven projects. Among the two laureates, one involves the CRCT:

PACMINE – A model of pancreatic carcinogenesis: from intrinsic to extrinsic factors.

Dr. Julie Guillermet-Guibert (CRCT team SigDYN) and Dr. Elisa Boutet (TOXALIM)

While the role of genetic alterations in the development of pancreatic cancer in exocrine acinar cells is known, the significance of these cells' environment (tumor niche) at the origin of the cancer (the cancer-initiating cell) is less well understood. Indeed, tissue microenvironment may possibly regulate cancer-initiating cells. The team hypothesizes that a modification of the mitochondrial metabolism of the niche is due to chemical pollutants (environmental contaminants) and has already identified a key protein (target) that also alters the niche.

The project has two objectives: i) seeing whether PC initiation can be triggered by a modification of the pancreatic parenchyma (niche) and of its mitochondrial metabolic activity via exposure to pollutants or inactivation of key regulator molecules, in order to propose new prevention strategies; ii) characterizing toxic exposure to pesticides as a factor potentially responsible for increasing PC incidence.

* The other project is led by Dr. Arnaud Besson (CBI) and Dr. Laurent Malaquin (LAAS CNRS): "Development of 3D micro-physiologic systems to study the fate of intestinal stem cells and model the first steps of tumorigenesis".

III

PATIENT CARE AND CLINICAL RESEARCH

Key figures

35,188 patients treated in 2020 including **10,007** new patients who came to the technical centers or to the consultation, radiotherapy or hospitalization departments.

3,342 patients received oral therapies (+9.6%)

105,237 hospital stays (-2.47%) including 54,574 radiotherapy sessions (-5.7%)

224 transplants (+19.8%) including 79 allogenic transplants (+9.7%) and **145** autologous transplants (hematology and solid tumors/ +16%)

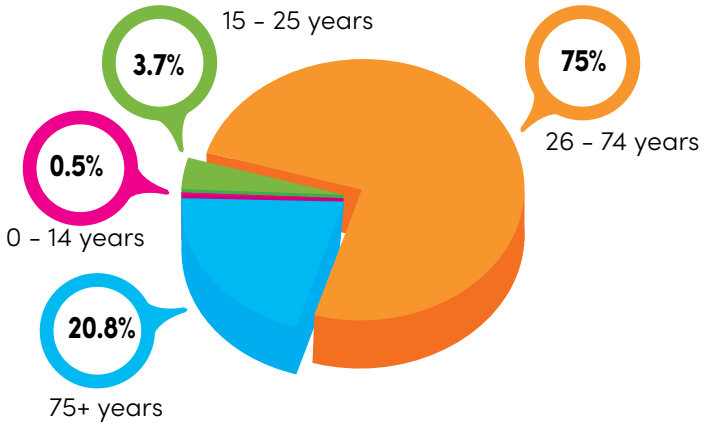
17 patients treated with CAR-T cells (+64.7% compared with 2019)

80.7% outpatients in the hospitalization departments

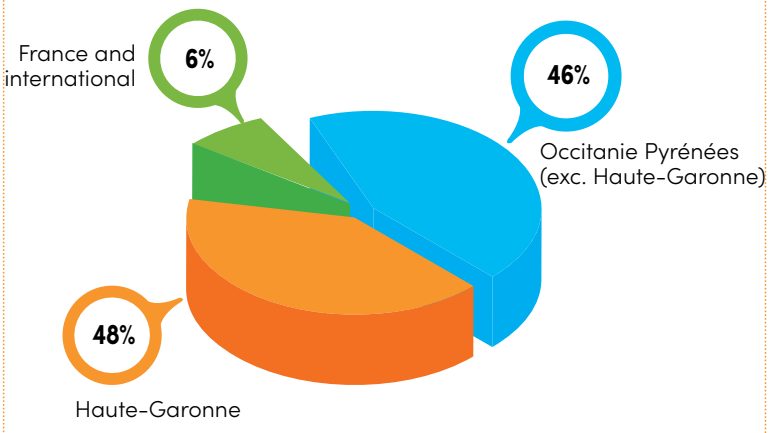
43.7% men – **56.3%** women

217 clinical trials included patients in 2020
1,517 IUCT-Oncopole patients included in clinical trials, that is **13.7%** of patients (active file)
38.4% were early phase trials

Distribution by age group



Geographical origin of patients



A care pathway a life pathway

IUCT-Oncopole patients benefit from a multi-disciplinary approach ensuring the best possible care: weekly multidisciplinary team (MTD) meetings discuss and study every patient's records to propose the most appropriate personalized and innovative support, education and rehabilitation.

Care for specific sectors of the population

Adolescents and young adults (AYA)

The IUCT-Oncopole is a NETSARC+ national referral center (INCa accredited) for bone sarcomas, a form of cancer that affects young patients (mean age at diagnosis = 15 years). NetSarc+ helps run a regional mobile coordination unit (AJAMIP) that provides support to hospital doctors, general practitioners, patients and their families, and ensures patient care is adapted to the needs of 15-25-year-olds. In addition, AYA patients have access to their own activities room (with a graffiti mural, video games, "pro" table football game, etc.), where they can relax in a fun and easy-going environment.

Older patients

Treatment pathways for older cancer patients are determined in the light of patients' overall health, their autonomy and their family situation. The Geriatric Oncology Organ Coordination Committee (OCC) takes into account all of these parameters when drawing up treatment programs, in order to find the best compromise between efficacy and the quality of life.

Testing customized prostheses!

In collaboration with the Toulouse start-up New Team Medical, Prof. C. Vaysse launched an original study to evaluate the potential benefits of a customized prosthesis making it possible to best adapt the weight, but also the skin "tone" or the aspect of the nipple.

Integrated and personalized supportive care

The IUCT-Oncopole is unusual among cancer centers in that it has a dedicated interdisciplinary Department of Supportive Care (DISSPO), whose transversal, multidisciplinary activities complement the work of the healthcare departments and the Organ Coordination Committees (OCCs). More than 40 professionals and 20 volunteers provide patients with the support they need throughout their treatment.

The weekly news magazine Le Point's top rankings for 2020 The IUCT-Oncocole is:

- 2nd for head and neck cancer care (3rd in 2019)
- 4th for breast cancer surgery (5th in 2019)
- 5th for leukemia care in adults (12th in 2019)
- 6th for gynecological cancer surgery (6th in 2019)
- 8th for skin cancer care (10th in 2019)
- 11th for lymphoma and myeloma care (16th in 2019)
- 7th for sarcoma and soft tissue surgery (new ranking 2020)

Adapted physical activities... including rugby!

The IUCT-Oncopole's Sport & Cancer Center is one of 25 such centers funded by CAMI Sport & Cancer and its partners across France. Opened in 2017, it offers cancer patients free access to specially designed physical activity sessions. The Stade Toulousain Rugby Club joined the program and since 2018 has provided sports therapy sessions at the Ernest-Wallon Stadium, actively supporting the Sport & Cancer Center. In addition, in 2017 Dr S. Motton initiated a novel way of using sport to help cancer patients when she founded and became president of France's first "wellness rugby club". Baptized "Rubies", the club brings together women cancer patients and caregivers for weekly games of 5-a-side rugby, which form part of a "sport and health" protocol promoted by the French Rugby Federation.

Digital innovations for patient home monitoring

The IUCT-Oncopole has launched several telephone monitoring systems aimed at detecting and managing complications and side effects as quickly as possible, both during and after onco-hematology treatments (CoACh and CoACH TCO for solid tumors; AMA1, AMATO and AMA-AC for hematology).

The "Mon E-suivi IUCT Oncopole" secure web app offers seven different programs covering surgery, oncology and hematology outpatient pathways, as well as nutritional monitoring for radiotherapy patients.

Another specific smartphone app developed for patients in Geriatric Oncology (Infinity®) offers a semi-automatic messaging system centered around a Chatbot. The app will make it possible to improve telephone monitoring by reducing the number of unnecessary calls.

Improve patient care through bioethics reflection

Prof. B. Couderc (Professor of Biotechnologies and head of the IUCT Ethics committee) joined the IUCT-Oncopole DISSPO in 2020. A member of the BIOETHICS team (4) of the UMR Inserm/ UPS 1027 (team leader: Dr E. Rial-Sebbag), she coordinates several projects. Supported by the Ligue contre le cancer, she set up a first study aiming to improve communication among the different healthcare professionals so that patients receive the best information possible and comply with their care plan, once they have given informed consent. An information video was made for patients to present somatic and constitutional genetic testing. A communication campaign will be launched in the first semester of 2021 to include general practitioners in the Occitanie-Ouest region.

"Health Partnerships"

The IUCT-Oncopole's healthcare staff, associations and users work together to continually improve the quality of patient care. Providing care is seen as a form of "healthcare partnership", based on co-leadership, co-construction and co-responsibility to benefit all IUCT-Oncopole patients.

Programs to help patients manage living with cancer

The IUCT-Oncopole was named by the Occitanie Regional Health Agency as the "sponsor and guarantor of the Transversal Therapeutic Patient Education Unit (UTEP) in Cancerology for the Occitanie Region". Coordinated by E. Arfé and Dr N. Caunes-Hilary, the unit ensures two missions: to develop therapeutic patient education (TPE) in Occitanie, and to continue implementing the platform specially created in 2015 for patients receiving oral chemotherapy. A patient expert is also responsible for carrying out the anticancer TPE program "Cancer and oral treatment: I'm dealing with it!" across the Occitane-Est region.

Under the impetus of Dr A. Huynh, TPE programs have also been specifically developed to accompany patients receiving hematopoietic stem-cell transplants (both pre- and post-transplant).

A Users' Center for associations

Several charities work closely with the IUCT-Oncopole, often through volunteers who offer patients moments of companionship and support. A Users' Center (Maison des usagers) set up at the heart of the IUCT-Oncopole provides a dedicated space where patients and their families can meet with associations.

The Occitanie Region has been particularly dynamic in 2020 supporting adolescents and young adults (AYA). A total of 20 associations strive daily to accompany patients in partnership with healthcare professionals.

The regional branch of the Ligue contre le cancer, based in the Oncopole's Community Center, also provides a range of services and information leaflets.

Launched in 2020, Bull'Info is a space hosted by users for users. Located near the Reception desk, it provides access to patients and caregivers to information in printed form or on-line.

Members of the « User's Project » in February 2020.

The "Users' Project" 2019-2022

The IUCT-Oncopole, through the Institut Claudius Regaud, wants patients, caregivers, patients' representatives and patients' associations to come together with healthcare professionals of every category to co-construct a project that will benefit all IUCT-Oncopole users. It is not only about users' exercising their rights, but also about supporting healthcare teams in managing sometimes complex processes via three main orientations:

- Organizing the discharge procedure by means of a personalized, interactive guide for every patient;
- Promoting the services provided by the Supportive Care OCC through partnership between patients, caregivers and healthcare professionals;
- To help create closer partnerships between patients, caregivers and health professionals.

Among the initiatives launched is the creation of a scenario for a 3D immersive video for new patients to understand the codes and references of cancer care. From 2021, virtual reality masks will be offered to patients to "visualize" their pathways.

Patients are offered the latest therapeutic innovations

Less than six months to translate a CRCT discovery into a clinical trial

Thanks to the close ties between the hospital's clinicians and the CRCT's research teams, along with CLIP^2 (INCa early-phase trials) accreditation, it takes less than six months for a laboratory discovery to be translated into a clinical trial at the IUCT-Oncopole.

An individualized therapeutic vaccine in preparation

With conclusive preclinical results, a first phase I clinical trial was launched at the IUCT-Oncopole, led by Prof. J-P. Delord in collaboration with Prof. C. Le Tourneau (Institut Curie in Paris), with patients newly diagnosed with HPV-negative head and neck cancer, locally advanced and having been surgically treated. The year 2020 was dedicated to screening patients and to creating a first individualized vaccine, administered in January 2021, a first in Europe.

Research projects in care will also be deployed at the IUCT-Oncopole, led by clinicians or other health professionals in an assessment process of practices and innovation.

CAR-T therapy comes to the IUCT-Oncopole

The first two Gilead and Novartis accreditations were obtained in 2019 thanks to wide-ranging collaborations steered by Dr P. Bories of the Onco-Occitanie network. Centered around the patient, several teams have joined forces to optimize patient care: the Hematology OCC (contact: Dr A. Huynh), the Intensive and Continuing Care Department (CAR-T cell contact: Dr M. Picart), the Neuro-oncology OCC (CAR-T cell toxicity contact: Dr D. Larrieu-Ciron), and the Pharmacy (contact: Dr A. Grand). The French National Blood Service's cytapheresis and cell therapy teams are also involved in the process, since they manage the harvesting, processing and dispatching of cells to pharmaceutical laboratories. Finally, collaborations with Toulouse University Hospital's neuroradiology team and electrophysiology unit ensure that brain MRI scans and ECGs are interpreted immediately in the case of toxicities.

Several developments in 2020:

- Indications were extended to include mantle cell lymphoma (ATU KTE X19) along with, as part of a phase III clinical trial (Kamma-3), myeloma.
- In collaboration with DISSPO and CAMI Sport & Cancer, physical activity programs adapted to pre-, per- and post- CAR-T cells have been set up.
- Medical data are now integrated in the DESCAR-T national register, promoted by LYSARC, for the purpose of better characterizing the efficacy and tolerance profile (both short- and long-term) in actual conditions of use.
- Finally, the IUTC-Oncopole participates in building a collection, housed at the Institut Carnot CALYM (the CeVi cryoconservation collection of viable human cells), of biological material from patients treated with CAR-T cells.

After the first eight patients in 2019, 17 new patients benefitted from this therapeutic innovation in 2020 despite the health crisis.

Quality clinical research

Member of numerous INCa clinical research networks

The IUCT-Oncopole is one of the first three members of the **Network of INCa-accredited early phase trials centers** (CLIP2, coordinator: Prof. J-P. Delord). In addition, the IUCT-Oncopole (through the Institut Claudius Regaud) has joined forces with the Bordeaux University Hospital, the Institut Bergonié and the Montpellier Regional Cancer Institute to set up a "Greater Southwest Network of Early Phase Trials Centers". The IUCT-Oncopole is also a member of the INCa-accredited "National Investigation Group for Studies of Ovarian and Breast Cancers" (**ARCAGY-GINECO**), which is presided by Dr L. Gladieff, who is also the GINECO coordinator for the IUCT-Oncopole. Prof. C. Laurent is the Lymphoma Study Association's (**LYSA**) regional coordinator, and Prof. E. Moyal, the regional coordinator for the National Preclinical Radiotherapy Research Network (**RADIOTRANSNET**).

Active member of the OncoDistinct international network

OncoDistinct is an international network of clinical research institutions that promotes innovative, multi-center studies aimed at accelerating the development of anticancer drugs, especially for conditions where no therapeutic standard yet exists. The network's 27 members include 12 Comprehensive Cancer Centers. Dr C. Gomez Roca is a member of the coordinating team.

Co-creator of the association SCOPP

Prof. J-P Delord is one of the co-creators of the association SCOPP – Academic Association for Developing Early-Phase Onco-Hematology Trials in France. Its objective is to ensure that patients receive rapid access to new drugs by bringing together clinicians specialized in early-phase trials and by promoting such trials in discussions with decision-makers, corporations and patients' associations.

Quality assurance procedures for research

- The Institut Claudius Regaud became France's first cancer clinical research establishment to obtain ISO 9001 certification in France, along with the Institut Paoli-Calmettes (in 2013).
- The Toulouse University Hospital was France's first university hospital to obtain ISO 9001 certification for its Research and Innovation Department (in 2015).

Beyond its methodological support for clinical trials, the biostatistics unit, coordinated by T. Filleron, develops methodological research aiming to improve statistical treatment of therapeutic trials in collaboration, particularly, with the Toulouse School of Economics.

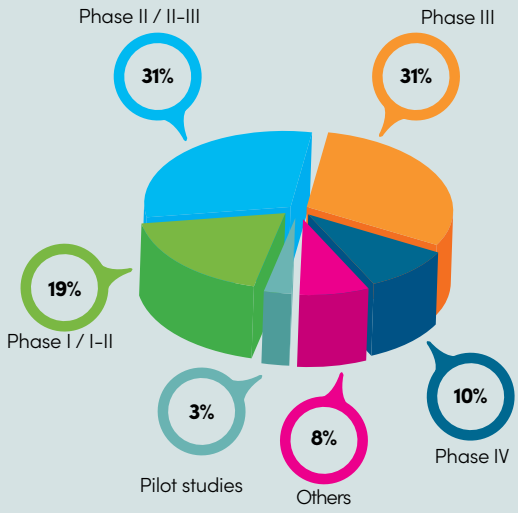
The main clinical research indicators

341 clinical trials open to inclusions in 2020

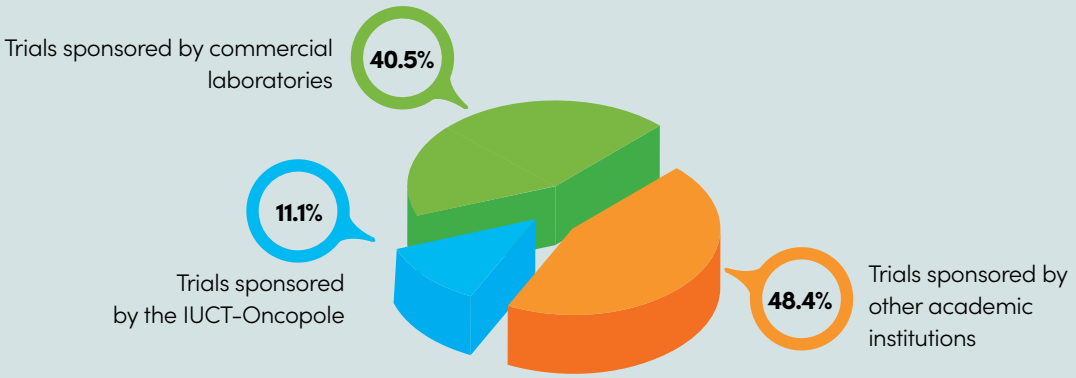
38.4 % early-phase trials **1,620** patients, including **1,517** IUCT-Oncopole patients (**13.7%** of the active file), included in a clinical trial in 2020

10.6% of clinical trials that included patients in 2020 were sponsored by the IUCT-Oncopole

Trials that included patients in 2020 : proportion by trial phase



Percentage of inclusions by sponsor type



The IUCT-Oncopole has signed several framework agreements to join international clinical research networks, such as the Global Expert Centers Initiative (GECI, Bristol-Myers Squibb), OTX (Novartis)... The IUCT-Oncopole is the first French center to have signed a Master Agreement with the imCore network (Genentech). A new multi-year agreement, "Alliance Oncopole", was signed with the Pierre Fabre Research Institute on the theme of personalized medicine. Finally, transfer agreements have been signed with a number of commercial companies, giving them limited access to datasets resulting from clinical trials.

Member of the European MyPeBS study

My Personal Breast Screening **(MyPeBS) is a Unicancer-coordinated, international study to evaluate a new screening strategy for breast cancer, based on a woman's individual risk of developing the disease. In total, 85,000 volunteers who have never had breast cancer will take part in the study (www.mypebs.eu).**

Organ Coordination Committees

To ensure that each patient receives the most appropriate integrated treatment according to her/his pathology, healthcare at the IUCT-Oncopole is organized around specialized Organ Coordination Committees (OCCs). These OCCs:

- define personalized treatment pathways and ensure that patients receive the best quality care;
- define the frequency and format of MDT meetings, in conjunction with France's network of Cancer Coordination Centers;
- suggest modifications on the way care is organized to the Patient Care Pathway Committee and identify needs in terms of personnel and equipment;
- organize clinical and translational research in their fields;
- help train experts and future professionals.

Fifteen OCCs have been set up and are listed below.

IUCT-ONCOPOLE OCC	
GYNECOLOGY	Dr. Laurence Gladieff
HEMATOLOGY	Prof. Christian Récher
SKIN CANCERS	Prof. Nicolas Meyer - Dr. Dimitri Gangloff
NEURO-ONCOLOGY	Prof. Elizabeth Moyal - Dr. Delphine Larrieu-Ciron
ONCOGENETICS	Prof. Rosine Guimbaud
GERIATRIC ONCOLOGY	Dr. Loïc Mourey - Dr. Laurent Balardy
HEAD AND NECK CANCERS	Prof. Sébastien Vergez - Dr. Anouchka Modesto
SARCOMAS	Dr. Christine Chevreau
BREAST CANCER	Prof. Florence Dalenc - Dr. Eva Jouve – Prof. Charlotte Vaysse
SUPPORTIVE CARE	Dr. Nathalie Caunes-Hilary - Prof. Virginie Woisard
THYROID & NEUROENDOCRINE CANCERS	Prof. Frédéric Courbon - Prof. Rosine Guimbaud - Prof. Delphine Vezzosi
UROLOGIC CANCERS	Prof. Bernard Malavaud - Dr. Loïc Mourey - Dr. Jonathan Khalifa
DIGESTIVE CANCERS	Prof. Rosine Guimbaud
PEDIATRIC ONCOLOGY	Prof. Anne Laprie - Dr. Marie-Pierre Castex – Prof. Marlène Pasquet
THORACIC CANCERS	Prof. Julien Mazières
DIGESTIVE CANCERS	Prof. Rosine Guimbaud
THORACIC CANCERS	Prof. Julien Mazières

IUCT-Oncopole patients with multiple pathologies or who develop complications are managed by the **Department of Internal Medicine.** Although this department is not, strictly speaking, an OCC, it is described as such in the following pages.

UCT-O OCC

BREAST CANCER

Coordinators: Prof. Florence DALENC, Dr. Eva JOUVE et Prof. Charlotte VAYSSE

Active file	***Active file, excluding oral therapies*** (change compared with 2019)
Total	**2,818** (+1.5%)
Surgery	**1,258** (-11.8%)
Chemotherapy	**1,138** (-3.5%)
Radiotherapy	**995** (- 6%)

45 specialists

34,332 hospital stays
(-3.6% compared with 2019)

42 trials open, including 3 phase I-I/II

STRATEGIC OBJECTIVES:

- Create a post-cancer consultation giving patients a Personalized After-Cancer Program (PPAC) after early-stage treatments;
- Reinforce clinical research at all stages of the disease and sponsor more clinical trials;
- Integrate translational research centered on metabolism and resistance to treatments, as well as research focusing on PARP inhibitor resistance mechanisms;
- Optimize regional cooperation on training and research.

• An "express pathway" for oncogenetics

The national timelines for oncogenetics for breast cancer patients are very long (at present around two years). In 2020, the OCC, together with the Oncogenetics Department, set up a fast track for metastatic patients for theranostic purposes (results in 15 days) and a semi-rapid track for patients with localized breast cancer treated with neoadjuvant chemotherapy and falling within the criteria of an oncogenetic investigation (results in three-four months).

• Development of innovative customized prostheses

The OCC is concerned with a specific, particularly difficult, period in patients' care pathway between mastectomy and secondary breast reconstructive surgery. To improve quality of life during these few months, Prof. C. Vaysse set up a trial, in collaboration with the Toulouse start-up New Team Medical, to evaluate the potential benefits of a customized external prosthesis (MEAVANTI), thanks to 3D innovations, making it possible to best adapt the weight, the skin "tone" of the prosthesis or the aspect of the nipple.

• Two principal themes of translational research

- **Metabolism & Cancer"**

Prof. C. Vaysse is part of the UMR 5089 whose aim is to characterize the role of the adipocytes surrounding the tumor in disease progression and the molecular mechanisms involved in obesity. A project was undertaken in collaboration with Dr C. Franchet on the extensive characterization of mammary adipose tissue (MAT), based on the hypothesis that the amplification of lipid transfer between adipocytes and tumor cells is one of the major mechanisms explaining the increased paracrine effect of MAT in the case of obesity.

- **Mechanisms of resistance to PARP inhibitors (PARPi)**

The OCC plans to set up, as of 2021, a national, prospective cohort of patients treated with PARPi to test whether tumor cell POLQ expression (as well as that of other proteins involved in DNA double strand break repair), as measured by RNAscope®, can explain primary or acquired resistance to PARPi, and whether the latter varies according to the nature of BRCA1/2 mutations.

Main collaborations: CRCT teams SIGNATHER (Prof. G. Favre/Dr O. Sordet), ONCOSARC (Dr F. Chibon) and DynAct (Dr S. Valitutti) plus UMR 5089 CNRS-IPBS (Prof. C. Muller) team "Microenvironnemnt Cancer et Adipocytes".

SELECTED PUBLICATIONS IN 2020:

. Mosele, F. et al. **Outcome and molecular landscape of patients with PIK3CA-mutated metastatic breast cancer**. Ann. Oncol. 31, 377-386 (2020).

. Pons-Tostivint, E. et al. **Radiation therapy to the primary tumor for de novo metastatic breast cancer and overall survival in a retrospective multicenter cohort analysis.** Radiother Oncol 145, 109-116 (2020).

. Prodhomme, M. K. et al. **EMT transcription factor ZEB1 represses the mutagenic POLθ-mediated end-joining pathway in breast cancers**. Cancer Res (2020)

. Puszkiel, A. et al. **Model-based Quantification of Impact of Genetic Polymorphisms and Co-Medications on Pharmacokinetics of Tamoxifen and Six Metabolites in Breast Cancer**. Clinical Pharmacology & Therapeutics cpt.2077 (2020)

IUCT-O OCC
GYNECOLOGY

Coordinator: Dr. Laurence GLADIEFF

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**937** (+16.5%)
Surgery	**365** (+10.3%)
Chemotherapy	**369** (+4.5%)
Radiotherapy	**104** (-1%)
Brachytherapy	**163** (-7.4%)

17 spécialists

6,161 hospital stays
(+ 10.8% compared with 2019)

18 trials open
including 2 phase I-I/II

The IUCT-Oncopole, via the Institut Claudius Regaud, is a European Society of Gynaecological Oncology (ESGO) accredited training center.

STRATEGIC OBJECTIVES:

- Treat peritoneal carcinomatosis (from initial characterization to palliative care);
- Perform complex surgery for pelvic relapse of gynecological cancers and reconstruction techniques;
- Explore the link between immunity and ovarian and cervical cancers;
- Perform minimally invasive surgery.

• Nationally recognized expertise

The IUCT-Oncopole, via the Institut Claudius Regaud, is an INCa-accredited "Regional referral center for rare malignant ovarian cancers" (TMRG) and a "Regional center of expertise" within the French Network for Rare Peritoneal Tumors (RENAPE). Through its members, the OCC is also affiliated to several leading cooperative groups and learned societies, notably the French Society for Gynecological Oncology (SFOG), the Inca-accredited National Group of Ovarian and Breast Cancer Investigators (ARCAGY-GINECO), and the Francophone Society for Oncological Surgery (SFCO), whose vice-president is Dr. G. Ferron. In 2020, several of the OCC's physicians helped draft the Saint Paul de Vence Guidelines for Clinical Practice, unveiled in January 2021 at the 19th Francophone Conference on Breast and Gynecological Cancers.

• Several research programs underway on ovarian cancer

To contribute to better characterizing different aspects of cancerogenesis, several translational research programs are proposed to patients when they begin therapy. Some are local, sponsored by the IUCT-Oncopole: DECIDE, whose aim is to describe the tumor immune environment, and PLATINOV, seeking to identify chemotherapy resistance mechanisms as well as new prognostic biomarkers capable of predicting treatment response. Other programs are national, such as GREAT, aiming for better understanding of the genetic profile of ovarian tumor cells.

• FEMINICOL: evaluate the benefits of sexological support

To evaluate the impact of including sexological support on the general and sexual quality of life of patients treated for cervical cancer by radiochemotherapy and brachytherapy, J. Ménard and Dr . A. Ducassou launched the prospective study FEMINICOL, including 60 patients in 2020. The study was financed by the Ligue régionale contre le cancer; its results are expected in 2022.

• Significant collaboration with the IMAGYN association

On the occasion of "Turquoise September", the OCC was approached by the IMAGYN association (Initiative of patients with gynecological cancers) to lead a webinar followed by more than 300 patients. Furthermore, IMAGYN included Dr. L. Gladieff in developing the free application "VIK Ovaire" whose aim is to accompany patients living with, and in understanding, their cancer. More than 1,800 people had downloaded the app by the end of 2020.

Main collaborations: CRCT teams T2i (Prof. M. Ayyoub and Prof. J-P Delord) and ONCOSARC (Dr. F. Chibon)

SELECTED PUBLICATIONS IN 2020:

. Angeles, M. A. et al. **Comparison of postoperative complications and quality of life between patients undergoing continent versus non-continent urinary diversion after pelvic exenteration for gynecologic malignancies**. International Journal of Gynecologic Cancer 30, 233–240 (2020).

. Martinez, A. et al. **Tumour and pelvic lymph node metabolic activity on FDG-PET/CT to stratify patients for para-aortic surgical staging in locally advanced cervical cancer**. Eur. J. Nucl. Med. Mol. Imaging (2020)

. Narducci, F. et al. **Severe perioperative morbidity after robot-assisted versus conventional laparoscopy in gynecologic oncology: Results of the randomized ROBOGYN-1004 trial.** Gynecologic Oncology 158, 382–389 (2020).

. Ray-Coquard, I. et al. **Effect of Weekly Paclitaxel With or Without Bevacizumab on Progression-Free Rate Among Patients With Relapsed Ovarian Sex Cord-Stromal Tumors: The ALIENOR/ENGOT-ov7 Randomized Clinical Trial.** JAMA Oncol (2020)

. You, B. et al. **Avelumab in Patients With Gestational Trophoblastic Tumors With Resistance to Single-Agent Chemotherapy: Cohort A of the TROPHIMMUN Phase II Trial.** Journal of Clinical Oncology JCO.20.00803 (2020)

IUCT-O OCC
SARCOMAS

Coordinator: Dr. Christine CHEVREAU

Indicators/Value (comparison with 2019)	
MDT meetings	**49**
Files	**1,177** (-0.42%)
Patients	**678** (+1.18%)

16 specialists

300 new patients per year

20 trials open, including 2 phase I-I/II trials

The OCC is a member of the IUCT's "Sarcoma/Bone Tumors" group, coordinated by Prof. P. Bonnevialle and Dr. C. Chevreau.

STRATEGIC OBJECTIVES:

- Continue to structure the provision of care for patients with soft tissue and bone sarcomas within the region;
- Develop its translational research activities by coordinating the national SARRA project and by working with the CRCT team ONCOSARC team to optimize the CINSARC genomic signature.

• A national center of expertise

The IUCT-Oncopole, through the ICR, is one of the 25 sarcoma expert centers and 15 bone referral centers of the "NETSARC+" network, validated once again by INCa in 2019, and now grouping together the various networks of expertise: clinical (NETSARC), anatomopathological (RRePS) and bone (GROUPOS), in which OCC "Sarcoma" physicians are involved.

• A very strong transversality in clinical care

The Sarcoma team is multidisciplinary with members from both the Institut Claudius Regaud and the Toulouse University Hospital and operates through the Sarcoma MDT. This high degree of transversality is necessary for patient care due to significant diversity in:

. the nature of tumors (malignant, intermediary malignancy, benign), since sarcomas actually include approximately 150 different histological forms;

. the necessary surgical expertise, since the pathology can occur anywhere in the body;

. the population concerned, sometimes occurring in AYA patients ("Adolescents and Young Adults"), with activity shared with oncopediatricians. In 2020, this structuring has become a reality and meets INCa requirements. It brings together the AYA groups – adult solid tumors (Dr. C. Chevreau), adult hematology (Dr. F. Huguet), pediatric solid tumors (Dr. M-P. Castex) and pediatric hematology (Dr. G. Plat).

• Development of specific care pathways

With the development of their routine use in other domains, the surgical team regularly uses pedicled perforator flaps in reconstructive surgery. In 2020, Dr T. Méresse initiated the creation of the "PERFOSARC" database to evaluate the reliability of these flaps in reconstructive surgery for soft tissue sarcomas of limbs and anatomical walls in adults. Moreover, preoperative radiotherapy for limb sarcomas, the standard treatment for initially inoperable tumors, is being evaluated in doctoral research from the perspective of adaptive radiotherapy. The results will change current care in the OCC, with particular attention paid to certain sub-types of sarcomas whose volume increases during treatment, and less intervention for tumors whose volume decreases, mainly myxoid liposarcomas. Another multicenter retrospective study is currently being analyzed; its aim is to study the role of radiotherapy in local recurrences of retroperitoneal sarcomas.

• Two new clinical trials launched in collaboration with the CRCT

Two clinical trials were launched in 2020 in collaboration with the CRCT. The CHIC trial evaluates the potential of the CINSARC signature to select patients at high metastatic risk and to assess the benefits of chemotherapy. The SAMHY trial is a pilot study to evaluate the rate of circulating cancer cells resulting from fusion with macrophages, a mechanism recently identified as potentially associated with metastatic development.

Main collaborations: Interconnections with the CRCT team ONCOSARC (Dr. F. Chibon); collaboration with GROUPOS and GSF-GETO/RESOS

SELECTED PUBLICATIONS IN 2020:

. Croce, S. et al. **The Nanocind Signature Is an Independent Prognosticator of Recurrence and Death in Uterine Leiomyosarcomas**. Clin Cancer Res 26, 855–861 (2020).
. Dufresne, A. et al. **Specific immune landscapes and immune checkpoint expressions in histotypes and molecular subtypes of sarcoma**. Oncolmmunology 9, 1792036 (2020).
. Maillard, M. et al. **Pharmacogenetic Study of Trabectedin-Induced Severe Hepatotoxicity in Patients with Advanced Soft Tissue Sarcoma**. Cancers 12, 3647 (2020).

IUCT-O OCC
HEMATOLOGY

Coordinator: Prof. Christian RECHER

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**1,950** (+14.6%)
Chemotherapy	**1,165** (-1.2%)
Radiotherapy	**123** (-6.1%)
Type of transplant	**N° hospital stays** (change compared with 2019)
Transplants	**224** (+19.7)
Allogenic transplants	**79** (+9.7%)
Autologous transplants	**145** (+26.1%)

14 specialists

16,390 hospital stays (+5.1% compared with 2019)

17 patients treated using CAR-T cells

105 trials open, including 17 phase I/I-II

STRATEGIC OBJECTIVES:

- Increase patient capacity;
- Extend outpatient treatment;
- Optimize cooperation with centers in the Onco-Occitanie-Ouest network;
- Develop early phase clinical research for intensive treatments (leukemia, CAR-T cells, HSC transplants) and evaluation (real-time molecular diagnosis, residual disease, clonal evolution);
- Develop real-world clinical research;
- Integrate translational research into clinical practice (molecular, phenotypic, functional and clonal descriptions of residual disease).

• A referral center within several French networks

The OCC is the Occitanie-Pyrénées region's referral center for hematology and is drafting, with the Occitanie-Méditerranée referral center, the regional referential for treating non-Hodgkin lymphomas. It is also a member of several French networks, including IFM, FILO, fi-LMC, GRAALL, FIM, SFGM-TC and LYSA. In 2020, the OCC obtained the European JACIE accreditation (Joint Accreditation Committee of ISCT-Europe and EMBT) for the quality of its care in hematopoietic stem cell transplants and cell therapy.

• Consolidation of CAR-T cell care

Two first accreditations were obtained in 2019. In 2020, indications were extended to include mantle cell leukemia (ATU KTE X19) along with, as part of a phase III clinical trial (Kamma-3), myeloma. After the first eight patients in 2019, 17 new patients were able to benefit from this therapeutic innovation in 2020. Medical data are now integrated in the DESCAR-T national register, promoted by LYSARC. The IUCT-Oncopole also participated in building a collection of biological material with the Institut Carnot CALYM.

• DATAML: a robust registry of myeloid leukemia

In 2009, Prof. C. Récher, in collaboration with Prof. A. Pigneux from the Bordeaux University Hospital, initiated a regional registry, DATAML, compiling data from more than 4,900 acute myeloid leukemia patients treated in Toulouse and Bordeaux. Collaboration with international groups is also ongoing. The aim is to be able to query this database for research projects to optimize medical practices (more than 40 publications since its creation). New databases on transplant and molecular biology, in connection with DATAML, are under construction.

• The launch of a personalized medicine project

The IUCT-Oncopole-ImCORE "THALYES" 2020-22 project was launched in 2020 in collaboration with ROCHE. Led by Prof. L. Ysebaert, working with CRCT team NoLymIT (coordinator: Prof. C. Laurent), THALYES 2020-22 will use biopsies from patients with lymphomas to create 3D tumor models in order to test drugs, and thus offer patients truly personalized treatments in the near future.

• Optimizing coordination of clinical trials in hematology

In 2019 the Hematology OCC appointed Dr. F. Despas to coordinate clinical trials. Dr. Despas will work with Prof. C. Récher to coordinate studies conducted in collaboration with Toulouse University Hospital's Clinical Research and Innovation Department and to strengthen cooperation with the IUCT-Oncopole's Office of Clinical Trials with respect to phase I trials in hematology. Seventeen studies have thus been launched in 2020.

Main collaborations: CRCT teams: NoLymIT (Prof. C. Laurent), GENIM (Prof. H. Avet-Loiseau and Dr. L. Martinet), ALTFAL (Prof. E. Delabesse) and METAML (Dr. J-E. Sarry)

SELECTED PUBLICATIONS IN 2020:

. Bories, P. et al. **Impact of TP53 mutations in acute myeloid leukemia patients treated with azacitidine.** PLoS ONE 15, e0238795 (2020).
. Corre, J. et al. **Del17p without TP53 mutation confers poor prognosis in intensively treated newly diagnosed multiple myeloma patients.** Blood blood.2020008346 (2020).
. Dumas, P.-Y. et al. **Delivering HDAC over 3 or 5 days as consolidation in AML impacts health care resource consumption but not outcome**. Blood Advances 4, 3840-3849 (2020)..
. Perrot, A. et al. **Health-Related Quality of Life in Transplant-Ineligible Patients With Newly Diagnosed Multiple Myeloma: Findings From the Phase III MAIA Trial**. JCO JCO.20.01370 (2020).
. Vercellino, L. et al. **Predictive factors of early progression after CAR T-cell therapy in relapsed/refractory diffuse large B-cell lymphoma**. Blood Adv 4, 5607-5615 (2020).

IUCT-O OCC
SUPPORTIVE CARE (DISSPO)

Coordinators: Dr. Nathalie CAUNES-HILARY et Prof. Virginie WOISARD

STRATEGIC OBJECTIVES:

- Implement supportive care as early as possible in care pathways;
- Refocus SOS activity on the most complex situations;
- Implement the Personalized After-Cancer Program (PPAC) in the different care pathways starting in 2021 with Breast cancer.

• A regional, national and European referral center

. At the request of the Occitanie Regional Health Agency, the IUCT-Oncopole coordinated a Transversal Therapeutic Patient Education Unit (UTEP) for cancer patients in the region.
. In 2020, the DISSPO participated in updating three referentials of the Association Francophone des Soins Oncologiques de Support (Francophone Association of Supportive Cancer Care - AFSOS) on cognitive disorders, fatigue and bereavement, as well as drafting a new referential entited "Pain and cancer: interventional radiology".
. Furthermore, the DISSPO social workers actively participate in Unicancer working groups on palliative care and social care. A white paper is planned for 2021.
. Finally, the OECI certification praised the DISSPO for its organization and its involvement in the various care pathways.

• Engaging closer to patients

. The year 2020 confirmed the complexity of patients' psychosocial situations and led to increasing even further the significant involvement of community healthcare professionals. In particular, the DISSPO formalized a partnership with the network of "breast physiotherapists" whose members commit to being trained in post-breast cancer physiotherapy and to maintaining regular practice.
. 2020 was also marked by the introduction of family mediation for patients and relatives facing family or intergenerational conflicts.
. Finally, since the health crisis prevented group sessions of adapted physical activities (APA) from taking place, the Sport & Cancer Center offered patients videos and on-line sessions at home.

• Conclusion of FEMINICOL and REFLEXISS studies

. The FEMINICOL project, coordinated by J. Ménard and Dr. A. Ducassou, ended in 2020. Its aim was to evaluate, over a two-year period, the benefits of a systematic introduction of onco-sexology in patients' care pathway, prior to brachytherapy in the case of gynecological cancers.
. A second project, REFLEXISS, also ended in 2020. Financed by INCa and carried out with the Federative Institute of Interdisciplinary Study and Research in Health and Society (FED 4142 – IFERISS), it explored how patients treated with oral anticancer drugs mobilize their know-how.

• Introducing a new research theme

Research by the DISSPO now also takes an ethical orientation with the arrival of Prof. B. Couderc, Professor of Biotechnologies, head of the IUCT Ethics committee and researcher in the BIOETHICS team 4 ("Trajectories of innovation in health: bioethic stakes and impact on public health, coordinator: Dr. E. Rial-Sebbag) of the UMR Inserm/UPS 1027. Thanks to ARC financing, two projects have been launched, respectively, on "The social pertinence and ethics of tele-consultations in cancer palliative care: a collaborative and interdisciplinary study" and on "Collegiality and implementation of deep and continuous sedation in cancerology".

Main collaborations: The IFERISS-CRESCO team (Prof. T. Lang) and UMR Inserm/UPS 1027 BIOETHICS team (Dr. S. Andrieu)

SELECTED PUBLICATIONS IN 2020:

. Couderc, B., 2020. **[George Lucas: prophet of transhumanism?]**. Med Sci (Paris) 36, 264–270.
. Kpoghomou, M.-A. et al. **Assessment of an onco-sexology support and follow-up program in cervical or vaginal cancer patients undergoing brachytherapy.** Support Care Cancer (2021)

IUCT-O OCC

HEAD AND NECK

Coordinators: Prof. Sébastien VERGEZ et Dr. Anouchka MODESTO

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**822** (+9.7%)
Surgery	**165** (-7.8%)
Chemotherapy	**297** (-0.3%)
Radiotherapy	**285** (-5%)
Brachytherapy	**19** (+18.8%)

15 specialists

9,808 hospital stays

(-2.7% compared with 2019)

22 trials open, including 3 phase I-I/II

STRATEGIC OBJECTIVES:

- Optimize care pathways;
- Develop knowledge-sharing activities;
- Increase research activities via three strategies: increase the number of trials, sponsor more clinical trials and extend OCC focus to include all areas of its activity through clinical trials.

• Regional referral center

The IUCT-Oncopole, in association with the IUCT-Larrey, is a referral center within the French Expert Network for Rare Head and Neck Cancers (REFCOR). The OCC plays a leading role in this network, notably thanks to its expertise in anatomical pathology and in sinus, cranial base and salivary gland surgery. In 2020, the weekly news magazine Le Point ranked the IUCT-Oncopole in 2nd place for head and neck cancer care.

• Production of regional and national guidelines

In 2020, in collaboration with the Onco-Occitanie network, the OCC updated the regional care guidelines for head and neck cancers. Furthermore, Dr. Dupret-Bories was involved in drawing up the national version of these guidelines (INCa), while Prof. S. Vergez helped update the national guidelines for sinus and nasal cancers (REFCOR) and was also named coordinator for updating salivary cancer recommendations. All of these guidelines will be published in 2021.

• 1st steps towards a personalized therapeutic vaccine

Having obtained conclusive preclinical results, a first phase I clinical trial was launched in 2020 at the IUCT- Oncopole by Prof. J-P. Delord in collaboration with Prof. C. Le Tourneau (Institut Curie in Paris). The aim is to create and evaluate a personalized therapeutic vaccine for patients newly diagnosed with HPV-negative head and neck cancer, locally advanced and having been surgically treated. The first step, consisting in screening patients and designing a vaccine, was carried out in collaboration with the OCC. A first patient will benefit from this innovative therapy offered by Biotech Transgene as of January 2021, a first in Europe.

• BIOFISS project, recipient of National Research Agency (ANR) funding

2020 saw Dr. A. Dupret-Bories obtain National Research Agency (ANR) funding for the BIOFISS project, in collaboration with two public research laboratories (CIRIMAT Toulouse and Inserm 1121, Strasbourg) and two industrial partners (Rescoll and Brothier Laboratories). The aim is to design an innovative algae-based bandage capable of reducing the risk of complications (salivary fistulae) in laryngectomized patients following head and neck cancer. The longer-term ambition is to commercialize the product in five years.

• COVID19: contribution to a guide for care guidelines

To respond to current preoccupations, Lionel Lami, a surgical nurse, contributed to drafting a guide (published in the American Journal of Critical Care – AJCC) reviewing the various precautions to take in caring for tracheostomized patients during the COVID pandemic. His shared experience within Surgery team 1B —very much invested in this question since the beginning of the SARS-CoV-2 epidemic— has thus benefitted others.

Main collaborations: CRCT teams T2i (Prof. M. Ayyoub and Prof. J-P Delord), RNA_{REG} (Dr. S. Millevoi) and the CIRIMAT - UMR CNRS INPT UPS 5085 Laboratory (Prof. C. Laurent)

SELECTED PUBLICATIONS IN 2020:

. Garrel, R. et al. **Equivalence Randomized Trial to Compare Treatment on the Basis of Sentinel Node Biopsy Versus Neck Node Dissection in Operable T1-T2N0 Oral and Oropharyngeal Cancer**. JCO JCO.20.01661 (2020)

. Le Tourneau, C. et al. **Phase I trial of Debio 1143, an antagonist of inhibitor of apoptosis proteins, combined with cisplatin-chemoradiotherapy in patients with locally advanced squamous cell carcinoma of the head & neck**. Clin Cancer Res clincanres.0425.2020 (2020)

. Mazerolle, P. et al. **Management of the irradiated N0-neck during salvage pharyngo-laryngeal surgery.** Eur J Surg Oncol (2020)

. Pandian, V. et al. **Critical Care Guidance for Tracheostomy Care During the COVID-19 Pandemic: A Global, Multidisciplinary Approach**. American Journal of Critical Care e1-e12 (2020)

IUCT-O OCC
NEURO-ONCOLOGY

Coordinators: Prof. Elizabeth MOYAL et Dr. Delphine LARRIEU-CIRON

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**358** (+10.2%)
Chemotherapy	**183** (+10.2%)
Radiotherapy	**188** (+8.7%)

5 specialists

5,792 hospital stays (+1.8%)

6 trials open, including 2 phase I-I/II

STRATEGIC OBJECTIVES:

- Develop integrated research to optimize treatment of brain tumors by studying the phenomena of radioresistance, by associating radioresistance pathway inhibitors, by improving ballistics and the definition of target volumes by multimodal imaging, and finally, by working on therapeutic response prediction by blood, tumor and imaging biomarkers.
- Propose inclusion in national or international clinical trials at every stage in patients' pathway.

• National and international recognition

The IUCT-Oncopole is an international referral center for neuro-oncology thanks to the innovative clinical trials that it either sponsors or participates in, especially phase I studies. The OCC is also a referral center for re-irradiation and has seen its activity increase by +157%, particularly through a national trial (STERIMGLI) of stereotactic re-irradiation combined with immunotherapy. Finally, Prof. E. Moyal was asked to co-sponsor the "S100A9-dependent radiation resistance in brain metastasis" project, funded by Worldwide Cancer Research. In this capacity, in close co-direction with Dr. A. Siegfried (Pathology Department), she supervised a dissertation in medicine. Finally, in 2020, Prof. E. Moyal was named an INCa national expert to participate in drafting the PAIR call for projects dedicated to brain tumors. She was given responsibility for the working group on "Therapeutic optimization".

• Member of referral networks

Prof. E. Moyal is a member of the Scientific Council of the European Association of Neuro-Oncology (EANO) and sits on the annual congress organizing committee since 2019. With Dr. D. Larrieu-Ciron of the Executive board of the French-speaking Association of Neuro-Oncologists (ANOCEF), she has also been a member since 2018.

• Research and therapeutic innovation

Since 2019 the IUCT-Oncopole has been able to provide CAR-T cell therapy to patients with hematological cancers. Introducing this new type of therapy has involved reorganizing patient care. Dr. D. Larrieu-Ciron has been tasked with coordinating responses to the complications and neurological toxicities associated with CAR-T cells.

• Research as part of the national POLA network

A national study on cohorts from the POLA network (affymetrix and clinical data - Toulouse coordinators: Prof. E. Uro-Coste and Prof. E. Moyal) has made it possible to compare, in patients with IDH-mutant anaplastic astrocytomas, radiotherapy + temozolomid chemotherapy to radiotherapy + PCV chemotherapy, since both treatments are proposed as therapeutic options. This study was the basis of a dissertation in medicine supervised by Prof. E. Moyal whose results, supporting the latter strategy, will be published in 2021.

• Follow-up of the SI2GMA project

The SI2GMA (Stereotactic Irradiation and Immunotherapy Glioblastoma Markers) project, led by Prof. E. Moyal and drawing on the data from the phase I-II STERIMGLI clinical trial, was selected in the Fondation ARC's first competitive grant scheme: SIGN'IT. It results from collaboration with the Radiotherapy and Medical Physics Departments, the Oncogenetics Laboratory, the Pathology Department, CRCT teams T2i (Prof. M. Ayyoub) and RADOPT (Prof. E. Moyal and Dr C. Toulas), and the Grenoble Institute of Neurosciences. A new axis of collaborative research has been established on the prediction of therapeutic response with specialists in artificial intelligence from the Technological Research Institute (IRT) Saint Exupéry.

Main collaborations: CRCT team RADOPT (Prof. E. Moyal and Dr. C. Toulas) and Inserm ToNIC team 1, unit 1214 (Dr. P. Péran)

SELECTED PUBLICATIONS IN 2020:

. Gouazé-Andersson, V. & Cohen-Jonathan Moyal, E. **New Avenues in Radiotherapy of Glioblastoma: from Bench to Bedside.** Curr Treat Options Neurol 22, 45 (2020).

. Kowalski-Chauvel, A. et al. **The m6A RNA Demethylase ALKBH5 Promotes Radioresistance and Invasion Capability of Glioma Stem Cells**. Cancers 13, 40 (2020).

. Larrieu, D. et al. **The E3 ubiquitin ligase TRIP12 participates in cell cycle progression and chromosome stability.** Sci Rep 10, 789 (2020)

. Roth, P. et al. **Neurological and vascular complications of primary and secondary brain tumours: EANO-ESMO Clinical Practice Guidelines for prophylaxis, diagnosis, treatment and follow-up**. Ann Oncol (2020)

IUCT-O OCC

ONCOGENETICS

Coordinator: Prof. Rosine GUIMBAUD

N° of consultations	(change compared with 2019)
1st consultation for a relative	**423** (-16.5%)
1st consultation for an index case	**684** (+4.4%)
Support and/or communication of results	**1167** (+31.6%)

7 specialists

2,707 consultations en 2019
126 cases presented in MDTs, including 75 for breast/ovarian syndromes and 51 for digestive syndromes

3 clinical trials specifically devoted to oncogenetics

STRATEGIC OBJECTIVES:

The Oncogenetics OCC is structured to respond to the region's (Occitanie-Ouest) needs in oncogenetics through consultations and genetic analyses performed on the Oncopole site, but also through the regional referral MDTs, the offer of pre-consultations in Rodez and Tarbes, training, and coordinating care in the community for individuals in the region with a hereditary predisposition to cancer.

- **Regional coordination to optimize diagnosis and patient care**

The Oncogenetics OCC also collaborates closely with IUCT-Purpan, IUCT-Rangueil/Larrey and the Onco-Occitanie regional cancer network to provide monitoring programs for breast-ovarian cancer syndromes, Lynch syndrome, familial adenomatous polyposis and hereditary endocrine neoplasias. Working groups have been set up with the oncogenetic consultation in Montpellier in 2020 to harmonize and optimize, throughout the region of Occitanie, indications for oncogenetic consultations and follow-up programs.
Coordinated by the Oncogenetics OCC, the GENEPY network brings together (under the aegis of Onco-Occitanie), facilitates and coordinates implementing optimal community care across the entire region of Occitanie-Ouest. This has been made possible through formal collaboration between oncogenetic consultations and physicians practicing in hospitals (private, public) or in community medical practices (298 professional members in total).

- **Implementing onco-hematologic coordination**

At the instigation of Dr. Pierre Vande Perre, the Oncogenetics OCC, the oncogenetic unit of the Oncology Medical Biology Laboratory (LBMO, coordinator: Dr. C. Toulas) and the "Genetics of hemopathies" unit (coordinator: Prof. E. Delabesse) of the Hematology Laboratory have joined together to propose a genetic onco-hematology care pathway. Concretely speaking, patients screened by the hematology laboratory in monitoring their leukemia will benefit from an oncogenetic consultation and a systematic search for blood-cell mutations by the LBMO. Where a hereditary mutation is found, family monitoring will then be undertaken.

- **Increasing activity**

The challenge for the OCC has been to implement specific circuits and adapt its activity to the significant increase in indications calling for therapeutically oriented genetic testing, at times as a matter of emergency, for therapeutic targeting of new molecules. Out of more than 50 French centers of oncogenetics, the IUCT-O is part of the "top 10" in the country with more than 2,500 consultations per year.

- **Launching an original research project in 2020**

In 2020, the OCC launched a study in collaboration with the CRCT team DIAD (coordinator: Prof. E. Chatelut) and the Biostatistics Cell of the IUCT-Onopole (coordinator: T. Filleron) aiming to identify predisposing factors of breast cancer in men.

Main collaboration: Pathology laboratory and Molecular Biology unit (director: Prof. P. Brousset)

SELECTED PUBLICATIONS IN 2020:

. Hamzaoui, N. et al. **Genetic, structural, and functional characterization of POLE polymerase proofreading variants allows cancer risk prediction.** Genetics in Medicine 22, 1533–1541 (2020).

. Lonjou, C. et al. **Gene and pathway level analyses of iCOGS variants highlight novel signalling pathways underlying familial breast cancer susceptibility.** Int. J. Cancer ijc.33457 (2020) doi:10.1002/ijc.33457.

. Surun, A. et al. **Medulloblastomas associated with an APC germline pathogenic variant share the good prognosis of CTNNB1-mutated medulloblastomas.** Neuro-Oncology 22, 128–138 (2020).

. Tjokrowidjaja, A. et al. **Concordance between CA-125 and RECIST progression in patients with germline BRCA-mutated platinum-sensitive relapsed ovarian cancer treated in the SOLO2 trial with olaparib as maintenance therapy after response to chemotherapy.** European Journal of Cancer 139, 59–67 (2020).

IUCT-O OCC
SKIN CANCERS

Coordinators: Prof. Nicolas MEYER et Dr. Dimitri GANGLOFF

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**751** (+6.4%)
Surgery	**477** (+13.8%)
Chemotherapy	**291** (+3.2%)
Radiotherapy	**100** (-16%)
Brachytherapy	**8** (+100%)

21 specialists

3,601 hospital stays (-15%)

14 clinical trials ongoing
including 4 phase I-I/II

STRATEGIC OBJECTIVES:

- The OCC is one of only a few units in France with the expertise to treat all neoplastic diseases (lymphomas, carcinomas, melanomas).
- Its research activities focus on improving the effectiveness of immunotherapy by remodeling the melanoma inflammatory environment, identifying biomarkers of responses to melanoma treatments and characterizing skin toxicities of cancer treatments.

• National and European referral center

The IUCT-Oncopole is a member of the INCa-accredited CARADERM network of hospitals for rare skin cancers (Merkel's carcinoma, adnexal carcinoma, basal cell carcinoma). In addition, Dr. V. Sibaud, in collaboration with Prof. G. Fabbrocini (Federico II University Hospital in Naples) and Dr. A. Freites-Martinez (Fuenlabrada University Hospital in Madrid), set up Europe's first network specializing in the dermatological toxicities of cancer treatments (ENCADO).

• State-of-the-art surgical techniques

The IUCT-Oncopole is one of only three centers in France to offer ganglion transfer surgery as a corrective procedure for refractory lymphedema, thanks to Dr. K. Kolsi, who has provided this innovative procedure since 2018. Moreover, the curettage of micrometastases is no longer carried out systematically, but is based on personalized indications according to the adjuvant treatment prescribed for each patient. The decrease in prophylactic surgery has resulted in decreased morbidity of initial treatment for melanoma. Moreover, a dissertation in medicine was begun in 2020 under the direction of Dr. T. Méresse examining the oncological safety of perforator flap reconstructive surgery. This innovative technique, taking effectively into account the anatomy and function of the areas in question, could replace the standard technique of direct structural excision.

• Further developments in patient care pathways

The year 2020, with the transfer of conventional hospitalization stays to the IUCT-Oncopole site, marked the last step in localizing all dermatological activity at the same location. In addition, protocols for home care were set up with the home hospitalization service for immunotherapy. Finally, the prevention of relapse was intensified using adjuvant protocols.

• Publication of several articles on immunothérapy

Several industrial trials were published in international journals in 2020, notably the first results of the TICIMEL study. Sponsored by the IUCT-Oncopole, the latter is a phase 1b trial aiming to evaluate security in administering nivolumab and ipilimumab in combination with either certolizumab or infliximab in patients with advanced melanoma. A retrospective study was also published with interesting results on preventing brain metastases by immunotherapy.

Main collaborations: CRCT teams SIGNATHER (Prof. G. Favre and Dr. O. Sordet) and MELASPHINX (Dr. B. Ségui and Dr. N. Andrieu)

SELECTED PUBLICATIONS IN 2020:

. Marcaillou, M. et al. **PD-1 inhibitors might limit the development of brain metastases in patients with advanced melanoma.** Melanoma Research 30, 580–589 (2020).

. Montfort, A. et al. **Combining nivolumab and ipilimumab with infliximab or certolizumab in patients with advanced melanoma: first results of a phase 1b clinical trial.** Clin Cancer Res clincanres.3449.2020 (2020) . Imbert, C. et al. **Resistance of melanoma to immune checkpoint inhibitors is overcome by targeting the sphingosine kinase-1.** Nat Commun 11, 437 (2020).

. Lacouture, M. E. et al. **Prevention and Management of Dermatological Toxicities Related to Anticancer Agents: ESMO Clinical Practice Guidelines†.** Ann Oncol (2020).

. Nikolaou, V. et al. **Immune checkpoint-mediated psoriasis: a multicentric European study of 115 patients from European Network for Cutaneous ADverse Event to Oncologic drugs (ENCADO) group.** J Am Acad Dermatol (2020)

IUCT-O OCC
GERIATRIC ONCOLOGY

Coordinators: Dr. Loïc MOUREY et Dr. Laurent BALARDY

Activity	(change compared with 2019)
N° of evaluations by Mobile Geriatric Oncology Team (EMOG)	**1,229** (-14.5%)
N° of evaluations by registered nurse practitioners	**119** (-19%)

6 specialists

In 2020, **22.2% of IUCT-O patients** were aged 75 or older at the time of the MDT (data extracted from the DCC (shared medical records system)

STRATEGIC OBJECTIVES:

- Meet the needs of older patients on all three IUCT sites by ensuring their access to the most appropriate care and most innovative therapies, wherever they first receive treatment.
- Develop hospital-family doctor communication, in collaboration with the regional cancer network, to improve patient monitoring and follow-up care via the Shared Medical Record System (*Dossier Communicant de Cancérologie* – DCC).
- Anticipate future challenges in geriatric oncology by sponsoring dedicated research projects.

• A key component in the Geriatric Oncology Coordination Unit (UCOG)

The Geriatric Oncology OCC, Toulouse University Hospital's Geriatrics Department and the Onco-Occitanie cancer network work together closely within the Midi-Pyrénées Geriatric Oncology Coordination Unit. Medical coordination is provided by a joint geriatrician/oncologist team, supported by an assistant attached to the regional cancer network. A Mobile Geriatric Oncology Team (EMOG) has also been created to provide specialist expertise to the IUCT's departments and other hospitals in the region.

• A Chatbot app to improve monitoring older patients

The Geriatric Oncology OCC developed a smartphone app based on a conversational chatbot able to analyze patients' responses to standardized questions in order to avoid unnecessary calls during telephone follow-up. Since its beginning in 2018, 82 patients have been followed-up in this fashion, 37 in 2020 alone. An instant messaging system now completes this communication tool in order to develop the hospital-city link and to improve coordination of patient care pathways. This tool thus makes it possible to share medical information in a secure manner with the patient, her/his entourage and visiting nurses.

• Creation of a geriatric oncology MOOC

The year 2020 marked the on-line availability of a MOOC entitled "Cancer in the elderly: understanding its specificities in order to provide better care". This MOOC is a joint venture between Occitanie's two Geriatric Oncology Coordination Units, with input from a working group of 54 healthcare professionals from throughout France. Nearly 2,000 healthcare professionals across France have participated in the first two sessions broadcast in 2020.

• Specialist research projects

The OCC coordinates the PHRC-K Fraction project whose aim is to predict the toxicity of chemotherapy as a function of bodily composition. In conjunction with the IUCT-Oncopole Methodology Department, it has also developed a free statistical tool (R package) specially for clinical trials involving older patients.
The OCC also sponsors the LYMPH-OLD project, laureate of a national Ligue contre le cancer call for projects in 2020. This prospective cohort study, carried out within the IUCT-O, will make it possible to evaluate the impact of chemotherapy treatments on functional autonomy and the quality of life of patients aged 75 or older with a malignant lymphoid hemopathy.

SELECTED PUBLICATIONS IN 2020:

. Garric M et al. **Impact of a comprehensive geriatric assessment on decision-making in older patients with hematological malignancies**. Eur J Haematol. 2020. Online ahead of print.
. Mourey L et al. **Taking care of older patients with cancer in the context of COVID-19 pandemic**. Lancet Oncol. 2020;21(5):e236.
. Piau A et al. **Access to individualized oncology care for older patients in complex healthcare networks**: The skilled nurse option. J Geriatr Oncol . 2020;11(5):899-901.
. Sourdet S et al. **Impact of the comprehensive geriatric assessment on treatment decision in geriatric oncology**. BMC Cancer. 2020;20(1):384.

IUCT-O OCC

THYROID AND NEUROENDOCRINE TUMORS

Coordinators: Prof. Frédéric COURBON, Prof. Rosine GUIMBAUD et Prof. Delphine VEZZOSI

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**303** (-10.6%)
Surgery	**35** (-14.6%)
Chemotherapy	**8** (+33.3%)
Radiotherapy	**20** (-4.8%)
Radioactive iodine	**215** (-16.3%)

22 specialists

855 hospital stays

(-1.4% compared with 2019)

6 clinical trials ongoing

STRATEGIC OBJECTIVES:

The OCC, created in 2018, results from collaboration between departments from a number of establishments. Treating neuroendocrine tumors brings together the IUCT-Rangueil's Digestive Department, the IUCT-Oncopole's Nuclear Medicine and Pathology Departments, the IUCT-Rangueil/Larrey's Endocrinology Department, and the IUCT-Purpan's Biology Pôle. The treatment of thyroid diseases brings together Toulouse University Hospital's Endocrinology, Head and Neck Surgery and Thoracic Surgery Units, and the IUCT-Oncopole's Nuclear Medicine Department and Head and Neck Surgery Unit.

• Nationally and internationally recognized expertise

Through CCO members, the IUCT-Oncopole is part of the National Study Group for Endocrine Tumors (GTE) and the three branches of the INCa ENDOCAN referral network: RENATEN (neuroendocrine tumors), THUTHYREF (thyroid cancers) and COMETE (cancers of the adrenal capsule). Dr. S. Zerdoud is a member of the European Association of Nuclear Medicine's (EANM) Thyroid Committee. The center Operates as a network between the ICR and the Toulouse University Hospital and is one of only four French centers certified by the European Neuroendocrine Tumor Society (ENETS). The newly accredited body, baptized "Toulouse University Centre of Excellence for Neuroendocrine Tumors", is coordinated by Dr. L. Dierickx and directed by Prof. R. Guimbaud.

• Contributing member of APTED

The OCC accompanied the creation, in 2009, of the Association of patients with neuroendocrine tumors (APTED). Dr. L. Dierickx is still a member of its Scientific Council. This highly active national association succeeded, in particular, in mobilizing government authorities to both provide and cover costs for certain treatments that had previously only been available abroad, and whose late repayment to hospitals compromised care for French patients.

• Specialist MDTs

The OCC organizes a specific MDT for neuroendocrine tumors (RENATEN referral MDT every two weeks, led by Prof. R. Guimbaud). Other thematic MDTs also take place: the neuroendocrine tumor molecular biology MDT meets every two months in collaboration with the Federative Institute of Biology (Prof. F. Savagner); the standard thyroid MDT meets every week, while the specialist referral thyroid MDT meets every two weeks (national TUTHYREF MDT), and the regional referral MDT for metastatic tumors convenes once a month.

• Ongoing research projects

Several research projects, conducted in collaboration with CRCT or i2MC teams are ongoing. The year 2020 was marked, in particular by obtaining funding from the Ligue contre le cancer for the OXYTHYR project, led by Dr. L. Vija (Analysis of metabolic derivatives of cholesterol in the human thyroid). Another project, led by Dr. L. Dierickx, evaluates the quality of life of patients by means of a questionnaire. Finally, Prof. F. Courbon coordinates a national registry of endocrine tumors treated with 177Lu DOTATATE (EPILUNET Registry). Prof. R. Guimbaud also launched a national cohort of advanced non-digestive neuroendocrine tumors treated by chemotherapy.

Main collaborations: CRCT teams CMATI (Dr. M. Poirot and Dr. S. Silvente-Poirot) and DIAD (Prof. E. Chatelut), Team 6 i2MC UMR 1048 Inserm/Universitey (Prof. A. Parini and Prof. D. Cussac)

SELECTED PUBLICATIONS IN 2020:

. Caron, P., Broussaud, S., Galano-Frutos, J. J., Sancho, J. & Savagner, F. **New variant (Val597Ile) in transmembrane region of the TSH receptor with human chorionic gonadotropin hypersensitivity in familial gestational hyperthyroidism**. Clin. Endocrinol. (Oxf) (2020)

. Dierickx, L. O., Séverine, B., Fatima, M., Amel, B. & Rosine, G. **Successful and Safe Treatment With 177Lu-DOTATATE (Lutathera) of Progressive Metastatic Pancreatic Neuroendocrine Tumor Under Hemodialysis**. Clin Nucl Med 45, e400–e402 (2020).

. Goichot, B. et al. **Management of thyroid dysfunctions in the elderly. French Endocrine Society consensus 2019 guidelines. Short version**. Annales d'Endocrinologie S0003426620300883 (2020)

. Rahabi, M. et al. **Divergent Roles for Macrophage C-type Lectin Receptors, Dectin-1 and Mannose Receptors, in the Intestinal Inflammatory Response**. Cell Rep 30, 4386-4398.e5 (2020).

IUCT-O OCC
UROLOGIC CANCERS

Coordinators: Prof. Bernard MALAVAUD, Dr. Loïc MOUREY et Dr. Jonathan KHALIFA

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**889** (-6.5%)
Surgery	**53** (-22.1%)
Chemotherapy	**364** (-3.7%)
Radiotherapy	**356** (+1.7%)
Brachytherapy	**41** (-50%)

17 specialists

10,861 hospital stays
(-3.2% compared with 2019)

35 clinical trials open
including 5 phase I-I/II

STRATEGIC OBJECTIVES:

- Develop a multidisciplinary approach (innovation, therapy, clinical research);
- Propose and develop conservative treatments (bladder, prostate);
- Provide expertise on specific sectors of the population (adolescents and young adults; older adults).

• National reference for cancer in men
The IUCT-Oncopole is an INCa-accredited referral center for prostate brachytherapy. The year 2020 marked the creation of the "testicle" MDT. Initiated by Dr. C. Chevreau in collaboration with Onco-Occitanie, this originally regional undertaking now operates on a national level.

• Internationally recognized expertise
The Urologic Cancers OCC is a world pioneer in en-bloc endoscopic resection of bladder tumors and is only one of a few teams in France to perform 3rd-generation remedial cryotherapy. In 2020, in collaboration with Dr. P. Sargos of the Institut Bergonié, Dr. J. Khalifa drew up GETUG-AFUD guidelines for radiotherapy modalities in conservative treatment of bladder cancer.

• An increasingly important role for tele-consultation
Faced with the difficult context imposed by the COVID 19 pandemic (patients' reticence to come to the hospital, transportation difficulties), the OCC very quickly set up tele-consultations by telephone. Building on this experience, as well as on the know-how acquired, the OCC now wants to develop this practice on a regular basis, particularly for follow-up consultations. Moreover, the first graduate nurse practitioner will be remotely monitoring patients treated with oral therapies for cancer of the prostate (hormonotherapy) or of the kidney (targeted therapy).

• Innovations in patient care
Stereotactic radiotherapy was proposed for the first time in 2020 to prostate cancer patients, making it possible to reduce the number of hypofractionation sessions from 20 (standard practice) to five (extreme hypofractionation). This protocol will be routinely offered as of January 2021. Moreover, the current trend leans towards a multidisciplinary, conservative approach in treating localized bladder cancers, rather than the traditional surgical protocol.

• Further development of industrial partnerships
In addition to its scientific and technical partnership with Olympus and the German company MAVIG, in 2020 the Urologic Cancers OCC signed a new contract with the Grenoble-based company KOELIS to co-supervise an "Industrial Contracts for Training through Research" (CIFRE) doctoral project on image analysis by machine learning.

• Starting the award-winning INCa PHRC-K project
Led by Dr. J. Khalifa, BLAD-RAD01 is a phase II clinical trial to evaluate consolidative radiotherapy as a partial or complete response to metastatic urothelial carcinoma of the bladder in patients with at most three residual metastatic lesions after first-line systemic therapy. The research design had to be modified to integrate immunotherapy in both treatment arms.

Main collaborations: CRCT team T2i (Prof. M. Ayyoub and Prof. J-P Delord) and CNRS team "Sphingolipids and Cancers" at the Institute of Pharmacology and Structural Biology (IPBS, Dr. O. Cullivier).

SELECTED PUBLICATIONS IN 2020:
. Diamand, R. et al. **External Validation of a Multiparametric Magnetic Resonance Imaging-based Nomogram for the Prediction of Extracapsular Extension and Seminal Vesicle Invasion in Prostate Cancer Patients Undergoing Radical Prostatectomy.** European Urology S0302283820307648 (2020)
. Meyrignac, O., Aziza, R., Roumiguie, M. & Malavaud, B. **Closing the Gap between Prostate Cancer and Deep Learning Detection Tools.** Radiology 295, E9-E9 (2020).
. Ploussard, G. et al. **Assessment of the Minimal Targeted Biopsy Core Number per MRI Lesion for Improving Prostate Cancer Grading Prediction.** J Clin Med 9, (2020).
. Ploussard, G. et al. **Survival Outcomes of Patients with Pathologically Proven Positive Lymph Nodes at Time of Radical Cystectomy with or without Neoadjuvant Chemotherapy.** Journal of Clinical Medicine 9, 1962 (2020)..

IUCT-O OCC
PEDIATRIC ONCOLOGY

Coordinators: Prof. Anne LAPRIE, Dr. Marie-Pierre CASTEX et Prof. Marlène PASQUET

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**485 patients** (+7.8%)
Surgery	**122 patients** (+11.9%)
Chemotherapy	**214** patients (+15.1%)
Radiotherapy	**35** (+1.7%)

15 specialists

3,941 hospital stays
(+2.23% compared with 2019)

121 clinical trials open
including 37 early-phase trials

STRATEGIC OBJECTIVES:

The Pediatric Oncology OCC was created in 2018 as the culmination of a long-standing arrangement under which treatment is shared between the Toulouse University Hospital (pediatric hematology-immunotherapy-oncology team, visceral, orthopedic and neuro-surgery teams, interventional pediatric radiology and neuroradiology team, pathology team and hemopathy laboratory) and the Institut Claudius Regaud (radiotherapy and nuclear medicine teams).

• New features for the benefit of patients

. The year 2020 saw the first nurse practitioner trained to manage oral therapies. Her work will begin early 2021.
. The OCC is also involved with the AJAMIP unit (see p. 55) coordinated by the OCC Sarcoma together with Onco-Occitanie. In the agreement signed with CAMI Sports & Cancer to develop specially designed physical activity sessions, a corresponding research protocol was proposed by Dr. G. Willson-Plat, funded by the regional Ligue contre le cancer.

• Innovative research projects

. The Pediatric Oncology OCC designs and conducts numerous regional, national and European clinical research projects. In terms of basic and translational research, two main themes are being investigated under the Integrated Research Action Program (PAIR):
- "Brain tumors, ballistics and cognition" led by Prof. A. Laprie
- "Leukemias" led by Prof. M. Pasquet
In 2020, the "EPENDYMOMICS project: a Multiomics Approach to Radioresistance of Ependymomas in Children and Adolescents", coordinated by Prof. A. Laprie, was awarded "the Jury's favorite" in the annual Unicancer Innovation Competition.

• An OCC involved in referral networks

. In 2020, Prof. A. Laprie coordinated the pediatric recommendations for radiotherapy, RECORAD, to be published in 2021 by the French Oncological Radiotherapy Society (SFRO). Finally, OCC members belong to the French Society for Children's Cancers (SFCE); notably, Prof. A. Laprie and Prof. M. Pasquet are members of the Scientific Council. Prof. A. Laprie and Prof. M. Pasquet are also members of the Academic Council of the Inter-university Diploma of Pediatric Oncology (DIUOP) coordinated by the Institut Gustave Roussy.

Main collaborations: CRCT team ALTFAL (Prof. E. Delabesse) and the DEVIN team (Dr. P. Péran) of UMR Inserm 1214 - ToNIC

SELECTED PUBLICATIONS IN 2020:

.Brunac, A. et al. **The combination of radiotherapy and ALK inhibitors is effective in the treatment of intraosseous rhabdomyosarcoma with FUS TFCP2 fusion transcript**. Pediatric Blood & Cancer 67, (2020).
.Carrie, C. et al. **Exclusive Hyper-fractionated Radiotherapy and reduced boost volume for standard-risk medulloblastoma: pooled analysis of the two French multicentric studies MSFOP98 and MSFOP 2007 and correlation with molecular subgroups.** International Journal of Radiation Oncology*Biology*Physics 108(5):1204-1217 (2020).
.Lambert, M. et al. **Plasma cystatin C is a marker of renal glomerular injury in children treated with cisplatin or ifosfamide.** Pediatr Blood Cancer (2020)
. Olivier Gougenheim, L. et al. **Pediatric randomized trial EORTC CLG 58951: Outcome for adolescent population with acute lymphoblastic leukemia.** Hematological Oncology 38, 763-772 (2020).

DEPARTMENT OF INTERNAL MEDICINE

Coordinator: Prof. Odile RAUZY

5 specialists

5,407 hospital stays
(+17.6% compared with 2019),
85.3% of which were day-hospital stays
Active file (hospitalization): 1,065 patients (+11,9% compared with 2019)

2,504 consultations (+12.7% compared with 2019), one-third of which were devoted to rare immuno-hematologic diseases

2,443 LBP transfusion sessions
(+17.1% compared with 2019)
544 non-scheduled acute cases treated, that is, 11.7% of cases

12 clinical trials open, including 4 phase II trials and 2 phase III international trials

STRATEGIC OBJECTIVES:

- Offer specialized care in the field of rare immune-hematologic diseases such as autoimmune cytopenia and hemoglobin diseases;
- Provide recognized expertise in myelodysplasic syndromes;
- Develop specific transversal activities, in particular dealing with immunologic complications resulting from cancers and their treatments, managing complex care pathways and polypathologies, and non-scheduled care.

• Multi-referral center for rare diseases

The Department of Internal Medicine, led by Prof. O. Rauzy, is one of four national referral centers for autoimmune cytopenia in adults (CeReCAI). A regional registry of these diseases was set up in 2016 (Prof. D. Adoue, Dr. G. Moulis), and in 2020 it took on a national dimension thanks to the quality of the epidemiological data collected and on which several publications have been based. The Department is a center of expertise for sickle cell disease, thalessemic syndromes and other rare red-blood-cell and erythropoietic pathologies, as well as for histiocytosis and immune deficits in adults. Joint research into the child-adult transition and a joint therapeutic education program (ETP) relating to these pathologies have been set up with the corresponding pediatric services. The latter was validated by the DGOS in 2020 and will be proposed to patients in 2021.

• Provision of services to other OCCs

The Department of Internal Medicine has four transversal missions:
. Provide advice on anti-infective measures (Dr. K. Delavigne);
. Manage emergency blood supplies (Dr. P. Cougoul);
. Coordinate immunotherapy toxicity MDT meetings (Dr. T. Comont, Dr. J. Dion);
. Manage complex pathways (D. Yerle).

• The anti-infective referral mission at the heart of activities in 2020

In 2020, all care pathways were reorganized because of the health context. Thus, the role of anti-infective referral included a supplementary mission of formalizing a care pathway with dedicated beds during the first wave of the epidemic. Similarly, the organization of home monitoring also adapted to the COVID-19 context. A dedicated 24-hour telephone line was set up to respond to questions from primary care health professionals or on-site teams. Furthermore, a vast awareness campaign on nosocomial risks and the importance of influenza vaccination was launched end of 2019/early 2020. The innovative offer of on-site, in-department vaccination met with great success. As the year went on, this preventive approach was reinforced by the COVID epidemic itself through the utmost importance given to barrier gestures to protect our patients and vaccinate care teams.

• A translational research project launched to understand the role of the immune system

Funding (30 k€) was awarded by the national Ligue contre le cancer to support Dr. T. Comont's project (CRCT team METAML) on the "immunome", exploring the role of the immune system in the physiopathology of myelodysplasic syndromes in order to envisage new treatments.

Main collaborations: CRCT team METAML (Dr. J-E. Sarry)/CERPOP EQUITY team, UMR 1295, Inserm/University Toulouse III-Paul Sabatier (Dr. M. Kelly-Irving and Dr. C. Delpierre).

SELECTED PUBLICATIONS IN 2020:

. Comont, T. et al. **Positivity rate of systematic bone marrow smear in patients over 60 years old with newly diagnosed immune thrombocytopenia**. Blood Advances 4, 2136–2138 (2020).
. Corfmat, M. et al. **Low dose IL-2 in patients with steroid-dependent dysimmune manifestations associated with myelodysplastic syndromes: a three-case report**. Rheumatology keaa696 (2020).
. Moulis, G. et al. **Significance of antinuclear antibodies in primary immune thrombocytopenia: results of the CARMEN registry.** Blood Advances 4, 1974–1977 (2020).
. Ollier, N. et al. **Nivolumab-induced eosinophilic fasciitis: a case report**. Rheumatol Adv Pract 4, rkaa001 (2020).
. Boumaza, X. et al. **Pulmonary mucormycosis following autologous hematopoietic stem cell transplantation for rapidly progressive diffuse cutaneous systemic sclerosis: A case report.** Medicine 99, e21431 (2020).

OCC
DIGESTIVE CANCERS

Coordinator: Prof. Rosine GUIMBAUD

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**2,542 patients** (-2.1%)
Surgery	**554 patients** (-14.37%)
Chemotherapy	**693 patients** (+6.29%)
Radiotherapy	**209 patients** (-10.3%)
Brachytherapy	**5 patients** (+0%)

14 specialists

12,571 hospital stays
(-7.79% compared with 2019)

25 clinical trials ongoing
including 4 phase I/I-II

STRATEGIC OBJECTIVES:

- The OCC activity addresses the full range of digestive cancers (tube and liver/pancreas) and the stages of screening-diagnosis-treatment.
- It includes areas of specific referral: screening for genetic forms of colorectal/gastric and pancreatic cancers, early diagnosis of pancreas/colorectal and liver cancer, gastroesophageal - pancreatic – hepatobiliary (including transplant) surgery, rectal and peritoneal, interventional radiology (including thermo-ablation, hepatic intra-arterial approach, radio-embolization...), systemic or intra-arterial cytotoxic treatments, and radiotherapy.
- Research activities focus on molecular markers and genetic instability of colorectal cancers, and on innovative therapies for pancreatic cancer.

. The constant progression of activity has led, in 2020, to an increase in day-hospital capacity in the Department of Digestive Cancers (IUCT-Rangueil). Moreover, two very active weekly MDT meetings (around 3,000 cases discussed for 2,000 different patients in 2020) in digestive oncology are complemented by specific MDTs for hepatocellular carcinoma (HCC) and molecular digestive cancer, bringing together the Department of Digestive cancers, the Molecular Biology unit and the Office of Early Clinical Trials.

. Since immunotherapy was validated for several indications by princeps trials published in 2020 (dMMR advanced colorectal cancers, advanced HCC, esophageal cancers resected after radio-chemotherapy, etc.), the immunotherapy pathway has been strengthened. In addition, numerous therapeutic trials are still ongoing both in early phases and in II/III phases, making it possible to assess strategies and/or access to new treatments.

. In 2020, the OCC began migrating genotyping activity towards the Auragene national platform (France Genomic Plan 2025) by regularly transmitting cases and participating in meetings to validate results. The "National Pol-E Cohort", supported by the French Federation of Digestive Cancerology (FFCD) and coordinated by Prof. R. Guimbaud, Prof. Selves and Dr Farés, was also launched. This will make it possible to inventory and characterize tumors (digestive or extra-digestive) with Pol-E gene mutations and to collect on-site samples. Finally, the largest national biobank for pancreatic cancers (BACAP) remains active with numerous studies submitted to the Scientific committee.

Main collaboration: CRCT team ImPACT (Dr. P. Cordelier)

SELECTED PUBLICATIONS IN 2020:

. André, T. et al. **Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer**. N Engl J Med 383, 2207–2218 (2020).

. Frere, C. et al. **Incidence of Venous Thromboembolism in Patients With Newly Diagnosed Pancreatic Cancer and Factors Associated With Outcomes**. Gastroenterology 158, 1346-1358.e4 (2020).

. Gerossier, L. et al. **PARP inhibitors and radiation potentiate liver cell death in vitro. Do hepatocellular carcinomas have an achilles' heel?** Clin Res Hepatol Gastroenterol (2020) doi:10.1016/j.clinre.2020.09.014.

. Hammel, P. et al. **Erythrocyte-encapsulated asparaginase (eryaspase) combined with chemotherapy in second-line treatment of advanced pancreatic cancer: An open-label, randomized Phase IIb trial**. European Journal of Cancer 124, 91–101 (2020).

. You, B. et al. **The official French guidelines to protect patients with cancer against SARS-CoV-2 infection**. The Lancet Oncology 21, 619–621 (2020).

OCC
THORACIC CANCERS

Coordinator: Prof. Julien MAZIERES

Activity	Active file, excluding oral therapies (change compared with 2019)
Total	**1,913 patients** (+7.41%)
Surgery	**260 patients** (-3.35%)
Chemotherapy	**692 patients** (+3.75%)
Radiotherapy	**407 patients** (+26%)

8 specialists

13,281 hospital stays (+3.64% compared with 2019)

20 clinical trials open for inclusions, including 2 phase I/I-II

STRATEGIC OBJECTIVES:

- Screening, early diagnosis, thoracic surgery, radiotherapy, targeted therapies and immunotherapies;
- Basic research activity concentrating on understanding resistance to treatment; translational research focussing on four themes: analyzing biomarkers, liquid biopsies, resistance to anti-EGFR and managing toxicities.

. The year 2020 signaled the completion of the feasibility study for the LUNG PREDICT project, launched under the Alliance Oncopole agreement between the IUCT-Oncopole and Laboratoires Pierre Fabre, signed in December 2019. LUNG PREDICT's objective is to incorporate deep molecular characterizations when diagnosing patients with lung cancer, in order to offer them personalized treatment. The pilot phase, conducted in 2019, involved developing the logistic, experimental and bioinformatic protocols necessary to evaluate the entire project's feasibility. The support study of 2020, including 80 patients, analyzed their different profiles (clinical, proteinaceous, mutational, transcriptomic and bioinformatic).

. The "LUNG-RESIST project –Understanding and overcoming adaptive resistance to third generation anti-EGR targeted therapies in bronchial cancers"–, led by Prof. J. Mazières, was launched in 2020.

. Finally, the Kobe project, led by Dr. N. Guibert, aims to take advantage of the supernatant obtained from bronchial endoscopic ultrasound in order to perform molecular biology analyses to complement and reinforce results from tissue and liquid biopsies. This project received funding from the Research and Innovation call for projects (ARI) of the Toulouse University Hospital.

Main collaborations: CRCT teams T2i (Prof. M. Ayyoub and Prof. J-P Delord), SIGNATHER (Prof. G. Favre and Dr. O. Sordet), DynAct (Dr. S. Valitutti), NetB(IO)^2 (Dr. V. Pancaldi)

SELECTED PUBLICATIONS IN 2020:

. Mazieres, J. et al. **Atezolizumab vs Docetaxel in Pretreated Patients with Non-Small Cell Lung Cancer: Final Results From the Randomized Phase II POPLAR and Phase III OAK Clinical Trials**. Journal of Thoracic Oncology S1556086420308029 (2020)

. Mazieres, J. et al. **Vemurafenib in non-small-cell lung cancer patients with BRAFV600 and BRAFnonV600 mutations.** Annals of Oncology 31, 289–294 (2020).

. Mazieres, J. et al. **Randomized Phase II Trial Evaluating Treatment with EGFR-TKI Associated with Antiestrogen in Women with Nonsquamous Advanced-Stage NSCLC: IFCT-1003 LADIE Trial**. Clin. Cancer Res. 26, 3172–3181 (2020).

. Mazieres, J. et al. **Health-Related Quality of Life With Carboplatin-Paclitaxel or nab-Paclitaxel With or Without Pembrolizumab in Patients With Metastatic Squamous Non–Small-Cell Lung Cancer**. Journal of Clinical Oncology 38, 271–280 (2020).

. Paik, P. K. et al. **Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations.** New England Journal of Medicine NEJMoa2004407 (2020)

. Rudin, C. M. et al. **Pembrolizumab or Placebo Plus Etoposide and Platinum as First-Line Therapy for Extensive-Stage Small-Cell Lung Cancer: Randomized, Double-Blind, Phase III KEYNOTE-604 Study**. Journal of Clinical Oncology 38, 2369–2379 (2020).

Medico-technical services

Twelve medico-technical departments provide support for the Organ Coordination Committees' patient care and research activities. They also use their state-of-the-art facilities to carry out their own research projects.

Medical Imaging Department

Head of department: Prof. Frédéric Courbon
Assistant head: Prof. Nicolas Sans
31,970 procedures (-15.7% compared with 2019) including 12,180 conventional nuclear medicine procedures, 8,323 TDM scans, 4,847 MRI scans, 4,839 x-rays, 2,231 ultrasound scans
9 trials open for inclusions, including 2 phase I/I-II

. The Medical Imaging Department contains a radiology service, a nuclear medicine service comprising a radiopharmacy unit and a vectorized internal radiotherapy inpatient unit, and a breast radiology service.
. The Medical Imaging Department's PET center has been awarded the European Association of Nuclear Medicine's (EANM) "European Center of Excellence" certification every year since 2015. Furthermore, the IUCT-Oncopole and the IUCT-Rangueil/Larrey have now pooled their resources to form the "Toulouse University Center of Excellence in Neuroendocrine Tumors", certified as a "European Centre of Excellence for Neuroendocrine Tumors" by the European Neuroendocrine Tumor Society (ENETS).
. Collaboration with the Toulouse University Hospital became even stronger in 2020 with the sharing of physicians in neuro- and breast cancer radiology. A framework agreement was also signed with the Médipôle Clinic to reserve specific time slots for IUCT-O patients.
. The year 2020 saw the digital transformation of the Nuclear Medicine Department with the implementation of both computerized prescriptions and the Radiological Information System (RIS). Teleradiology has also been developed on-site due to the pandemic, in particular for TDM (19% of total scans) and cerebral MRI (7.8% of all MRIs).
. In terms of equipment, the Department replaced its scanner with a new apparatus whose technology improves tissue characterization (spectral imaging). A second PET scanner was installed using three new tracers: fluoroethyl estradiol (in a clinical trial), 68.GaPSMA and 18FAXUNIN. Furthermore, a clinical trial was launched in 2020 to study the use of 177LuPSMA in new therapeutic activities.
. The Department of Medical Imagery of the IUCT-O is the world validation center of General Electric Healthcare for their new generation of TEP scans (framework agreement signed in 2018). In 2020, a trial was launched to compare IQ et MI systems that should make it possible to set up new technology in 2021. Previously, however, a virtual lesion insertion technique was validated by the team, thanks to an ICR-GEHC doctoral student, with the aim of clinically assessing this new technology.
. The year 2020 also saw the conclusion of the HORIZON 2020 MEDIRAD project, thus ending the Department's partnership. Coordinated the by European Institute of Biomedical Imaging Imaging (EIBIR, Austria), the MEDIRAD project was based on a consortium of 33 partners from 14 European countries whose aim was to explore the effects of weak doses of radioactivity. Among the medical applications concerned is the use of iodine-131 in treating thyroid cancers (WP3 – coordinator: Glenn Flux). The IUCT-Oncopole is the only French establishment participating in the clinical research (coordinator: Prof. F. Courbon).
. Finally, the department is also examining the possibilities offered by artificial intelligence, most notably via a project launched by Dr. S. Kanoun to "train" a computer to recognize tumors from PET images. Other projects are being conducted with the Pathology Laboratory (machine learning on microscope and PET-scan images, in collaboration with Prof. C. Laurent) and the Medical Physics Department (automatic contouring structures for radiotherapy in collaboration with Dr. S. Ken and Dr. L. Simon).

SELECTED PUBLICATIONS IN 2020:

. Leray, H. et al. **FDG-PET/CT identifies predictors of survival in patients with locally advanced cervical carcinoma and para-aortic lymph node involvement to increase treatment**. J. Nucl. Med. (2020)
. Manceau, C. et al. **MRI Characteristics Accurately Predict Biochemical Recurrence after Radical Prostatectomy**. J Clin Med 9, (2020).
. Martinez, A. et al. **Tumour and pelvic lymph node metabolic activity on FDG-PET/CT to stratify patients for para-aortic surgical staging in locally advanced cervical cancer**. Eur. J. Nucl. Med. Mol. Imaging (2020)
. Meyrignac, O., Aziza, R., Roumiguie, M. & Malavaud, B. **Closing the Gap between Prostate Cancer and Deep Learning Detection Tools**. Radiology 295, E9–E9 (2020).
. Rossi, C. et al. **Baseline SUVmax is related to tumor cell proliferation and patient outcome in follicular lymphoma.** haematol 0–0 (2020)
. Vallot, D. et al. **Evaluation of PET quantitation accuracy among multiple discovery IQ PET/CT systems via NEMA image quality test.** EJNMMI Physics 7, 30 (2020).

Nuclear Medicine and Brachytherapy Hospitalization Unit

Unit head: Prof. Isabelle Berry
906 hospital stays excluding treatment sessions
231 brachytherapy stays (-20.3% compared with 2019)
434 Selective internal radiation therapy - SIRT patients (-5% compared with 2019)

. France's largest vectorized internal radiotherapy unit has 18 individual rooms with video monitoring and background radiation measurement. Thirteen of these rooms (including three day-hospital rooms) are used for vectorized internal radiotherapy; the other five rooms are used for brachytherapy.
. Moving away from iodine-131 to more easily manageable radioisotopes in treating thyroid cancers has shortened hospital stays since 2013 without compromising radiation protection standards. The unit's expert staff, who are particularly attentive to patient comfort, and top-quality facilities (including a high capacity for decontaminating liquids and solids) ensure that every patient receives the best possible care. Hospitalization should again increase in the coming years with the introduction of new recommendations (radium-223) and new authorizations for certain radioisotopes for prostate cancer, probably as of 2021 (177Llu-PSMA-617).
. The unit's main activity centers around treating thyroid cancer (241 patients in 2020), in collaboration with Prof. F. Courbon and Dr. S. Zerdoud, but also hyperthyroidism (203 stays in 2020). Nevertheless, its inpatient activity is becoming more varied and now includes treating bone metastases of prostate cancer and, more recently, neuroendocrine cancers. These have been treated on a routine basis under the impulsion of Dr. L. Dierickx since clinical trials were successfully completed in 2017. The IUCT-Oncopole is now a center of excellence in caring for this condition, with 75 stays in 2020.
. A complementary clinical, geriatric and onco-geriatric approach makes it possible to offer coordinated and comprehensive care to this primarily elderly, fragile and comorbid population.
. The unit has sponsored or participated in several ongoing clinical research projects in 2020, enabling, for example, the use of 177Lu-PSMA-617 in treating neuroendocrine tumors of pancreatic origin —an indication up until now not reimbursed and therefore unattainable for patients. The list of projects follows:

- the VISION project, led by the Institut Gustave Roussy, aims to assess the use of 177Lu-PSMA-617 in treating patients with progressive and PSMA-positive metastatic castration-resistant prostate cancer. Inclusions were stopped in 2020.
- an open, non-randomized multicentric phase I study to evaluate the biodistribution of radium 223 in participants with bone metastatic castration-resistant prostate cancer receiving radium 223-dichloride treatment (opened in August 2020).
- the ESTIMABL3 study, led by the Institut Gustave Roussy, to evaluate the impact of prophylactic central compartment neck lymph node dissection on results for differentiated thyroid cancers at low risk of loco-regional recurrence (recruitment underway).
- the multicentric phase III INTERMEDIATE_01 trial, led by the Centre François Baclesse and part of the TUTHYREF network, comparing two strategies in patients presenting a differentiated thyroid cancer (recruitment underway).
- the GENBIOLuNET project, led by Dr. L. Vija Racaru, involves measuring variability in molecular biomarkers that can be used to characterize radio-nucleotide therapies (Lu-177 DOTATATE) administered to patients with metastatic neuroendocrine tumors of the stomach and lower intestine (recruitment underway).

. New protocols are called for, notably to study neuroendocrine tumor treatment. Since the IUCT-O is the only center with pediatric authorizations in the Grand Sud-Ouest, in 2021 it will sponsor a clinical trial to evaluate the safety of irradiation with radiolabeled peptides (177Lu-DOTA0- Tyr3-Octréotate) in children's recurrent refractory metastatic neuroblastomas.

SELECTED PUBLICATIONS IN 2020:

. Dierickx, L. O., Brillouet, S., Mokrane, F., Bensafi, A. & Guimbaud, R. **Successful and Safe Treatment With 177Lu-DOTATATE (Lutathera) of Progressive Metastatic Pancreatic Neuroendocrine Tumor Under Hemodialysis.** Clin Nucl Med 45, e400–e402 (2020).
. Vija Racaru, L. et al. **Management of adenomas and toxic multinodular goiters with Iodine 131**. Médecine Nucléaire 44, 272–276 (2020).

Surgery Department

Head of department: Prof. Sébastien Vergez
Assistant head: Dr. Alejandra Martínez
7 operating rooms, including one devoted to R&D
5,292 patients (-0.13% compared with 2019)
7,596 operations (+0,64% compared with 2019), 2,036 of which were to place or remove a port-a-cath or CVC

. The Surgery Department's operating suite has seven operating rooms, two conventional wards (50 beds) and a day surgery ward (15 beds). Its objectives include extending outpatient surgery and perfecting surgical techniques and equipment.
. Thanks to a partnership with Olympus, one of the operating rooms is equipped with a 3D imaging system. Other innovative techniques used at the IUCT-Oncopole include robotic surgery, hyperthermic intraperitoneal chemotherapy (HIPEC), 3D-printer-assisted mandibular and maxillary bone reconstruction, preoperative radiotherapy (for breast cancers) and focal cryotherapy (for prostate cancer).
. Despite the pandemic —and unlike many other establishments having interrupted their surgical activity—, the department was able, thanks to effective internal reorganization, to take charge of all patients, nonetheless leaving facilities available in necessary to handle COVID patients.
. The weekly news magazine Le Point's top rankings for 2020 placed the IUCT-Oncopole 4th for breast cancer surgery (5th in 2019). Gynecological cancer surgery remains, as in 2018 and 2019, in 6th place.
. Dr. S. Leclerc and Dr. A. Martínez are both members of the Unicancer group entitled "Improved After-Cancer Rehabilitation" and organized the second national seminar. In this spirit, the department has recently introduced an improved post-surgery rehabilitation program for gynecological cancers that promotes rapid recovery over a short period of hospitalization, so patients are more independent when they go home. It complies with national and international guidelines (GRACE, ERAS, etc.) and includes Internet-based e-monitoring to enhance the safety of pre- and post-operative care.
. In collaboration with the MHComm company, the secure smartphone app "Mon E-suivi IUCT Oncopole" was officially launched in January 2019, following a pilot study supported by INCa and coordinated by Dr. A. Daboussi (PICTA), carried out in day surgery with 35 patients. The mobile app includes seven programs specifically adapted for outpatient care pathways in surgery, oncology, hematology and for nutritional monitoring in radiotherapy. Originally proposed to breast cancer patients, it will gradually be offered to patients with other cancers treated at the IUCT-Oncopole.

SELECTED PUBLICATIONS IN 2020:

. Barthes, J. et al. **Biofunctionalization of 3D-printed silicone implants with immunomodulatory hydrogels for controlling the innate immune response: An in vivo model of tracheal defect repair**. Biomaterials 268, 120549 (2020).
. Dahan, L. S. et al. **Mucoepidermoid carcinoma of salivary glands: A French Network of Rare Head and Neck Tumors (REFCOR) prospective study of 292 cases.** Eur J Surg Oncol (2020)
. Martinez, A. et al. **Tumour and pelvic lymph node metabolic activity on FDG-PET/CT to stratify patients for para-aortic surgical staging in locally advanced cervical cancer**. Eur. J. Nucl. Med. Mol. Imaging (2020)
. Pons-Tostivint, E., Alouani, E., Kirova, Y., Dalenc, F. & Vaysse, C. **Is there a role for locoregional treatment of the primary tumor in de novo metastatic breast cancer in the era of tailored therapies?: Evidences, unresolved questions and a practical algorithm**. Crit Rev Oncol Hematol 157, 103148 (2020).

Anesthesiology Unit

Manager: Dr. Régis Fuzier
Assistant manager: Dr. Geneviève Salvignol
4,198 consultations and 3,934 patients (–11.4% compared with 2019)
4,678 anesthesia procedures of all kinds except local (-5.9% compared with 2019)
2,036 procedures to place a port-a-cath or CVC

. In addition to providing anesthesiology services to all of the IUCT-Oncopole's departments, the unit is responsible for providing medical care to patients in the surgery department. It also works with the Quality Department on improving communication between stakeholders. Several members of the Anesthesiology unit are involved in various commissions or committees of the Institute: the Physicians' representative body (CME), Pain control committee (CLUD), the Committee for the culture of security.
. The unit is a leader in developing local-regional analgesia techniques for use in conjunction with general anesthesia to manage pain more effectively, especially in breast surgery and as part of morphine-sparing strategies. Doctors from all around the world come to the anesthesiology unit to learn these innovative techniques.
. In 2020, two permanent physicians were appointed (Dr. B. Combres and Dr. O. Staes), as well as an assistant physician (Dr. G. Pledel).
. In order to satisfy the various missions set by general management in addition to the conventional activities outlined above, several axes of work were determined in 2020: drawing up an action plan to develop interventional radiology (leader: Dr. Ph. Izard), developing interventional pain management (leader: Dr. M. Brémaud), furthering work on outpatient surgery (leader: Dr. B. Combres), implementing postoperative rehabilitation programs in the various surgical specialties (leader: Dr. S. Leclerc), contributing to reflection on disability (leader: Dr. G. Salvignol), complete re-evaluation of techniques and procedures for implanting long-term intravenous devices (leader: Dr. C. Cabos), implementing preoperative rehabilitation protocols in head and neck surgery, notably based on physical activity (leader: Dr. L. Nguyen), establishing procedures in the operating suite to reduce the ecological impact of waste (leader: Dr. O. Gilbert).
. The Anesthesiology unit participates in several clinical research projects. Analysis of the impact study on locoregional analgesic techniques after breast-conserving surgery was finished in

2020; an article is currently in preparation. Several team members will participate in the national PHRC study comparing the paravertebral block to the erector spinae muscle block in post-mastectomy analgesia. Finally, a national study among different CLCCs (French Comprehensive Cancer Centers) on managing vascular approaches was carried out in 2020, with results being presented by Dr C. Cabos during the first GARO (oncological anesthetist-ICU physicians) congress.

. The Anesthesiology team is strongly involved in both on-site training (IUCT-Oncopole paramedical healthcare teams) and external education (various university and inter-university diplomas). Drs. Ph. Izard and R. Fuzier are significantly involved in training in safety culture and human factors within the Institut, but also on a national level (Human Factors in the Field of Health Group, the Analysis and Risk Management Commission of the French Society for Anesthesia and Intensive Care). Episodes four and five of the "Dr. Captain Time" video were uploaded in 2020 (www.gifh.eu). In collaboration with the Quality Department, two training sessions were added to the catalog: a one-day course on the importance of non-technical competences and a five-day modular course on safety culture. In December 2020, nine healthcare professionals (physicians and paramedical health professionals) from the Bordeaux Institut Bergonié benefitted from the course on non-technical competences on board an Airbus 320 simulator.

. In 2020, the Anesthesiology team published a certain number of studies. Particularly noteworthy is the team's participation in developing recommendations for the European Anesthesiology Society on the role of ultrasound-guided vascular access. Similar guidelines will be drawn up in 2021 for anesthesia and locoregional analgesia.

SELECTED PUBLICATIONS IN 2020:

. Aveline, C., Fuzier, R., Lupescu, R., Choquet, O., & members of the i-ALR Association. **A prospective multicentre observational study on perioperative analgesia practices for total knee arthroplasty in France: the KNEEONE survey.** Br J Anaesth 124, e26-e28 (2020).

. Belbachir, A., Fuzier, R. & Biau, D. **Unexplained pain after scheduled limb surgery.** Orthop Traumatol Surg Res 106, S13-S18 (2020).

. Lamperti, M. et al. **European Society of Anaesthesiology guidelines on peri-operative use of ultrasound-guided for vascular access (PERSEUS vascular access)**. Eur J Anaesthesiol 37, 344-376 (2020).

Intensive and Intermediate Care

Manager: Dr. Jean Ruiz
12 beds
507 patients and 602 admissions (+6.5% compared with 2019), including 424 from the IUCT-Oncopole (45.4% from surgery, 54% from hematology and internal medicine)

. "Mieux Vivre en Réanimation" is a continuous improvement program aimed at making the intensive care experience as agreeable as possible for patients. The Intensive and Intermediate Care Department has taken numerous measures to achieve this, including holding multidisciplinary ethics meetings and allowing families to visit their relatives at any time on any day. Action to ensure effective and informative communication with patients and their families, and between caregivers, has also born fruit.

. A new initiative launched in 2020 has been very much appreciated: the department sends condolences to the families of deceased patients. Certain relatives have expressed their satisfaction and have also asked for an appointment to talk with the team. Reorganization projects are also underway, notably a children's playroom or information films.

. The quality of patient care within the department is also measured by the availability of healthcare teams. The department has organized itself to provide one Registered nurse for every 2.5 patients in intensive care and one for four patients in intermediate care (compared to six as a national average). To satisfy this objective, two intermediate care beds were transformed into intensive care.

. Several research projects are ongoing, notably in collaboration with the Respiratory Intensive Care in Onco-Hematology Research Group (GRRR-OH). The PICT project led by the Hôpital Saint-Louis on pneumocystosis and corticosteroid treatments is underway in 2020, as well as the DéPOH project sponsored by the Institut Paoli-Calmettes focusing on antibiotic de-escalation in onco-hematology for septicemia or septic shock. Discussions are ongoing with industrial partners to set up new trials in 2021.

. The Intensive and Intermediate Care Department is sponsoring a prospective, observational study of the factors considered when deciding whether to limit or discontinue treatment for intensive care patients aged 70 years or older. Baptized LATOId, this multi-center study involves eight intensive care departments across France and will include 900 patients.

. In terms of training, Dr. J. Ruiz intervenes in the Anti-infective chemotherapy university diploma at the University of Toulouse III-Paul Sabatier. Moreover, one of the department's nurses is a member of the paramedical Scientific committee of the French Society for Anesthesia and Intensive Care (SFAR) and is responsible for disseminating information on this learned society's paramedical training courses.

. Finally, the project for a pedagogical film on a surgical patient's pathway in intensive care received financial support for production from the Toulouse University Hospital. This is a collaborative effort between different surgical units and the Intensive and Intermediate Care Department, coordinated by the department's head nurse and two nurses.

SELECTED PUBLICATION IN 2020:

COVIDSurg Collaborative. **Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans: Elective surgery during the SARS-CoV-2 pandemic**. Br J Surg (2020).

Radiotherapy Department

Head of department: Prof. Elizabeth Moyal
54,754 radiotherapy sessions (-5.77% compared with 2019), 80% of which were IMRT
37 total body irradiation sessions (-26% compared with 2019)

. The Radiotherapy Department keeps fully up to date with innovations and advances in treatment: the IUCT-Oncopole was the first center in France to provide adaptive tomotherapy. In 2020, for its eighth bunker, it acquired Halcyon technology, integrating a particle accelerator and a scanner, thereby optimizing intensity-modulated image-guided radiotherapy. The department thus benefits from all of the cutting-edge technologies in radiotherapy, with seven complementary, recent apparatuses. In collaboration with the Engineering and Medical Physics Department (DIPM), dosimetric studies are performed to determine the most appropriate apparatus indicated in function of a patient's pathology and clinical condition.

. Additionally, a research project was launched in 2019 in collaboration with the DIPM and the Varian company to develop a new apparatus optimizing treatment, all the while preserving at-risk organs, particularly for neurological tumors. Early results were presented in an abstract and a poster at the annual American Society for Radiation Oncology (ASTRO) congress.

. Since its creation in 2018, the department is very much involved in the INCa network for structuring preclinical research in radiotherapy, RADIOTRANSNET. Prof. E. Moyal, member of the scientific steering committee, has intervened in several workshops. The last of these, in December, focused on the theme of tumor microenvironment and radiotherapy.

. The department accompanies several projects coordinated by the OCC and directs several trials and research projects, some of which are:

. ARION is a phase II clinical trial (sponsored by Dr. A. Modesto in collaboration with the Digestive Cancers OCC and 11 other centers in France) to evaluate associating radiotherapy/chemotherapy with immunotherapy (Durvalumab) for non-resectable esophageal cancer. The study is being carried out under Unicancer's and the French Cancer Federation's (FFCD) PRODIGE digestive cancer research partnership.

. SI2GMA (sponsored by Prof. E. Moyal), funded by the Regional Health Agency SIGN'IT program, examines predictive factors for responses to combined hypofractionated stereotactic re-irradiation with immunotherapy in patients with recurrent glioblastoma.

. SILK (coordinated by Prof. E. Moyal and Dr. J. Khalifa) is a trial to evaluate the effectiveness of combining stereotactic radiotherapy with immunotherapy in patients with progressive oligometastatic lung cancer on Durvalumab.

. The BLAD-RAD01 project, funded by the 2018 PHRC grant and sponsored by Dr J. Khalifa, is assessing the efficacy of consolidative radiotherapy in patients with a metastatic urothelial carcinoma of the bladder.

. The department is thus strongly involved in both clinical and upstream translational research in radiobiology (close links with the CRCT team RADOPT), as well as in metabolic and functional imaging for radiotherapy.

. The department also constantly seeks to improve and optimize its patient care. To this end, as well as to minimize the risk of error, weekly "Quality" meetings are held. Radiotherapy protocols have also been drafted in 2020 for each organ and disease, thanks to collaboration among physicians, medical physicists and dosimetrists. These elements, validated by the OCC, were praised by the French Authority for Nuclear Safety (ASN).

. Other evolutions in patient care have been implemented over the last few years, such as receiving treatment under hypnosis to reduce anxiety about radiotherapy, or moderately hypofractionated protocols for treating prostate cancer.

. Finally, the OECI audit found that, among the many sites visited over the last five years, the IUCT-Oncopole Radiotherapy Department was a notable example in terms of quality and safety of patient care and integrated research.

SELECTED PUBLICATIONS IN 2020:

. Cohen-Jonathan-Moyal, é., Vendrely, V., Motte, L., Balosso, J. & Thariat, J. **Radioresistant tumours: From identification to targeting**. Cancer/Radiothérapie S1278321820301669 (2020)

. Daguenet, E. et al. **To exploit the 5 'R' of radiobiology and unleash the 3 'E' of immunoediting: 'RE'-inventing the radiotherapy-immunotherapy combination.** Therapeutic Advances in Medical Oncology 12, 175883592091344 (2020).

. Dalmasso, C. et al. **Survival estimation of melanoma patients with brain metastasis using the Melanoma-molGPA score: external validation from a French cohort**. Melanoma Research 30, 472–476 (2020).

. Khalifa, J., Fléchon, A. & Chevreau, C. **Brain metastases from germ cell tumor: time to reconsider radiotherapy?** Critical Reviews in Oncology/Hematology 150, 102946 (2020).

. Modesto, A. et al. **Tolerance and efficacy of dose escalation using IMRT combined with chemotherapy for unresectable esophageal carcinoma: Long-term results of 51 patients**. Cancer/Radiothérapie 24, 88–92 (2020).

Pharmacy

Manager: Dr. Jean-Marie Canonge
Assistant manager: Dr. Florent Puisset
France's largest cancer hospital pharmacy in terms of chemotherapy preparations.
126,000 chemotherapy preparations, consisting of 116,000 standard chemotherapy preparations and 10,600 preparations for clinical trials for the IUCT-Oncopole, the oncology departments at Toulouse University Hospital-Purpan, Toulouse University Hospital-Rangueil/Larrey, Joseph Ducuing Hospital and HAD (home hospitalization) Santé Relais Domicile.
48,000 anticancer chemotherapy prescriptions
148 pharmaceutical consultations and 563 medication reconciliations for oral anticancer drugs

. Despite the particular context of the year 2020, overall activity was nearly identical to that of 2019, exception being the new clinical trials that could not begin during the first lockdown. The Pharmacy, of course, adapted its activity to the emergency Covid 19 situation. In a context of stock-outs, linked to a lack of visibility, the Pharmacy team was able to reorganize its activities and human resources to remain as close as possible to departments and patients.
Foremost, the Pharmacy's Covid 19 activities revolved around logistic questions, maintaining reliability of supply sources in healthcare products but also in personal protective equipment (masks, gowns, mobcaps, gloves), in accompanying departments in distributing equipment with the help of the Direction of nursing services and the Hygiene Service. The Pharmacy was also strongly mobilized in producing hydroalcoholic solution. Furthermore, arrangements were made for outpatients to offer local delivery at home or to a neighborhood pharmacy, including for patients participating in clinical trials. Innovative activities, like CAR-T cells, however, were maintained with no interruption.
. During the pandemic, the Pharmacy was able to maintain the safety of its preparation circuit by introducing video monitoring of chemotherapy preparation procedures for both standard and clinical trial preparations.
This innovative system, called Drug Cam, uses image processing techniques to check the most critical stages of the preparation process. Drug Cam monitors 60% of production for standard chemotherapy preparations and 100% of production for clinical trial preparations.
. The Pharmacy continues to develop its evaluations of currently used drugs. Using pharmacokinetic and pharmacodynamic data to individualize doses, especially for patients at risk (transfer of individualization tools developed by research projects), is also a priority.
. Finally, due to COVID 19, and in particular the first lockdown, the Pharmacy had to extend its competences in personalized protective equipment, as well as mobilizing to monitor supplies of essential drugs in short supply, in order to provide equivalencies or advise departments on concentrations or dilutions to avoid errors. Activity was subsequently very intense to make up for treatment delays built up during the first lockdown.

SELECTED PUBLICATIONS IN 2020:

. Azam, C. et al. **Association between clinically relevant toxicities of pazopanib and sunitinib and the use of weak CYP3A4 and P-gp inhibitors**. Eur. J. Clin. Pharmacol. (2020)
. White-Koning, M. et al. **Formulae recently proposed to estimate renal glomerular filtration rate improve the prediction of carboplatin clearance**. Cancer Chemother. Pharmacol. (2020)
. Pelagatti, V. et al. **[Adverse effects of contrast media: results of a 6 months study]**. Therapie 55, 391–394 (2000).

Oncology Medical Biology Laboratory (LBMO)

Coordinator: Prof. Gilles Favre
. 782,872 examinations (-0.04% compared with 2019) and 8,392,659 class-B procedures: (+1.64% compared with 2019)
. Decrease of 4.9% in RIHN* procedures compared with 2019, including Oncogenetics: 11,504,380 (-0.3% compared with 2019), Prospective biology: 411,000 (-39.4% compared with 2019), Pharmacology: 82,100 (-78.8% compared with 2019) and Rapid-response biology (immuno-assays, biochemistry): 61,810 (-1.59% compared with 2019)
. 97.2% of examinations were accredited by governmental authorities

. The Oncology Medical Biology Laboratory is divided into five units: Rapid-response Biology (Dr. L. Malard), Pharmacology (Prof. E. Chatelut), Immune Monitoring (Prof. M. Ayyoub), Oncogenetics and Pharmacogenetics (Dr . C. Toulas) and Prospective Biology (Dr. A. Pradines). The overwhelming majority of the Laboratory's activities (98%) are certified by France's accreditation agency (COFRAC). In addition, four CRCT teams share directors with the LBMO: Prof. M. Ayyoub for the T2i team, Prof. G. Favre for the SIGNATHER team, Dr. C. Toulas for the RADOPT team, and Prof. E. Chatelut for the DIAD team.
. The Oncogentics Unit has developed gene panels for susceptibility to a variety of cancers (breast/ovarian, digestive, pancreatic, melanomas, prostate). All of these panels, as well as tests for BRCA1 and BRCA2 tumor mutations in "fast track pathways" implemented in collaboration with the Pathology Laboratory, have received COFRAC accreditation. Moreover, since 2019, the Unit has been carrying out a systematic search for the TP53 gene prior to any radiotherapy in young women with breast cancer. The year 2020 saw the implementation of automated preparation for high throughput sequencing libraries. Also in 2020, the Oncogenetics unit launched a project to identify colon cancer genes found in young patients, as well as another project where the LBMO takes part in clinical studies with the Office of Clinical Trials. To meet these growing needs, a full-time post has been created to manage samples taken during clinical trials at the IUCT-Oncopole. Among the national trials underway in which the LBMO participates figure COVAR (classify variants of cancer susceptibility genes whose signification is unknown), TUMOSPEC (identify breast and ovarian cancer susceptibility genes other than BRCA), GREAT (study the genes involved in ovarian tumors' responses to PARP inhibitors) and a project to identify predispositions to breast cancer in men.
• The Prospective Biology Unit is highly involved in clinical research, innovation and the medical-economic evaluation of liquid biopsies for cancers. It contributes to translational research by managing a technical center (NanoString Technologies) and by developing original research projects directly linked to the CRCT, notably its own projects in close collaboration with the CRCT team SIGNATHER (leader: Prof. G. Favre) aimed at developing new circulating biological markers. The Prospective Biology unit, since 2018, has contributed to the PADA-1 research project (sponsored by Unicancer) by carrying out digital PCR analyses to detect ESR1 mutations in circulating tumor DNA. PADA-1 was set up to evaluate the tolerance and effectiveness of a combined Palbociclib-hormone therapy treatment for patients with metastatic breast cancer. The unit also takes part in a translational study

*RIHN: Schedule of reimbursements for innovative biological procedures

related to PADA-1, YODA, led by Prof. F. Clément-Bidard (Institut Curie). The Prospective Biology Unit is also a partner in the LUNG-RESIST project to understand and prevent adaptive resistance to EGFR tyrosine-kinase inhibitors in lung cancer. Led by Prof. J. Mazières (Thoracic Cancers OCC/CRCT team SIGNATHER), LUNG-RESIST is funded by a PRT-K grant. In 2020, the Prospective Biology Unit acquired, specifically for this project, a new imaging station equipped with a micro-manipulator making it possible to isolate cells for single cell transcriptomic studies. Finally, the unit is involved in the BIOLICAN project associating the LAAS-CNRS, the Pierre Fabre Research Institute, the CRCT and the IUCT-Oncopole. It aims to develop an innovative device capable of detecting molecular signatures of clinical interest in blood samples to enable early diagnosis of the disease.

. The Pharmacology Unit continues its research on tyrosine kinase inhibitors (either drugs with marketing authorization or under development). The year 2020 saw publication in Clinical Pharmacokinetics of the first studies in collaboration with the Hematology Department, particularly on the question of the pharmacokinetics of ibrutinib and PK-PD modelization of lymphacytosis. Projects underway explore pharmacogenetic/pharmacokinetic relations, one of which is PHACS - Pharmacokinetics of tamoxifen and aromatase inhibitors, correlation with pharmacogenetic characteristics, published in 2020. The Pharmacology Unit, moreover, is one of the first academic teams to avail itself of pharmacokinetic population analysis, exploring its use for radiotracers in a theranostic perspective —one where pharmacology has until now been little considered. In its everyday activities, Therapeutic Drug Monitoring of methotrexate has made it possible to better describe optimal use of glucarpidase to prevent kidney damage from high-dosed methotrexate and to question dose calculation of this drug in function of the body surface area of obese patients. Research projects on the theme have thus been launched, and one of them, in collaboration with the Department of Medical Imaging, has been funded by a national program for in-hospital clinical research (PHRC). Other research projects are also underway with the Unicancer "Genetics and cancer" group.

. The Immuno-monitoring Unit aims firstly to identify biological parameters associated with clinical response to immunotherapies and assure appropriate follow-up in dedicated clinical trials. But ancillary studies to clinical trials are also underway: CITHARE (Dr A. Modesto) and STERIMGLI (Prof. E. Moyal). Working directly with the CRCT team T2i, the unit has set up its own trials, such as the MINER study (Prof. J-P. Delord and Prof. M. Ayyoub) to monitor immune resistance mechanisms and response biomarkers in patients with various types of cancer (lung, bladder, head and neck) treated by immunotherapy. Lung and bladder cohorts began to be recruited in 2018, coordinated, respectively, by Prof. J. Mazières and Dr. D. Pouessel. Building the head and neck cancer cohort is coordinated by Prof. J-P. Delord and Dr. C. Gomez Roca. A further study, DECIdE, led by Dr. A. Martinez and Prof. M. Ayoub, began to recruit patients in 2020 and aims to analyze, in patients with several types of cancer (ovarian, cervical, head and neck, etc.), spontaneous immune response against their tumor prior to any therapy to predict the types of tumors likely to respond to immunotherapies. Early results, published in collaboration with the Pathology Laboratory and the Surgery and Medical Oncology Departments, have made it possible to show that T CD8+ and T CD4+ "depleted" lymphocytes (that is, that express immune checkpoints targeted by immunotherapies) are specific to tumor antigens, and that the presence of depleted LT C8+s correlates with a better response to immunotherapy. To carry out all of these projects, the Immuno-monitoring Unit benefits from support by the imCORE network, the MSDAVENIR foundation, the ARC Foundation, the Ligue contre le cancer and AstraZeneca and Bristol-Meyers Squibb.

SELECTED PUBLICATIONS IN 2020:

. Gallais, F. et al. **Population Pharmacokinetics of Ibrutinib and Its Dihydrodiol Metabolite in Patients with Lymphoid Malignancies**. Clinical Pharmacokinetics 59, 1171–1183 (2020).

. Guibert, N., Pradines, A., Favre, G. & Mazieres, J. **Current and future applications of liquid biopsy in nonsmall cell lung cancer from early to advanced stages.** Eur Respir Rev 29, (2020).

. Puszkiel, A. et al. **Model-based Quantification of Impact of Genetic Polymorphisms and Co-Medications on Pharmacokinetics of Tamoxifen and Six Metabolites in Breast Cancer**. Clinical Pharmacology & Therapeutics cpt.2077 (2020)

Hematology Laboratory

Manager: Prof. Eric Delabesse

. The Hematology Laboratory covers three main fields (cellular hematology, hemostasis and onco-hematology), combining biology and clinical practice, divided into 11 distinct workflows in five technical platforms (automated platforms at the Purpan, Rangueil and IUCT-Oncopole sites, a specialized platform at Purpan, a specialized onco-hematology platform at the IUCT-Oncopole). The activity is carried out by 15 biologists (four university professor-hospital practitioners, two associate professor-hospital practitioners, seven hospital practitioners and two university hospital assistants) in close collaboration with clinicians in adult and pediatric hematology, as well as the on-site Internal Medicine Department.

. For the IUCT-O, routine analyses (complete blood count and hemostatis testing) have increased by +15% since 2015 and have slightly decreased since 2019 (-0.8%). 3,490 myelograms were read in 2020, an average of 14 myelograms per workday (+6% progression compared with 2019).

. The Onco-hematology Transfer Platform includes two functional entities: the Hemopathy genetics unit (all blood cancers except for myeloma) and the Myeloma genomics unit (myeloma alone). In 2020 it performed 37.6 million procedures, hemopathy genetics accounting for 20.6 million procedures (+7%) and myeloma genomics for 17 million procedures (+8%).

. Cytometric analysis procedures in hemopathy genetics increased by 17% to 5.3 million. The number of requests for cytometry grew by 11% in 2020 to reach 8,204 analyses (158 per week). Molecular biology procedures increased by 12% to 12.4 million analyses, with the number of requests progressing by 6% in 2020 to 8,913 analyses (171 patient files per week). Cytogenetic requests increased by 9% in 2020 to reach 3,538 samples (68 patient files per week), leading to the analysis of 2,711 samples (+6% progression, mainly due to increasing demand from the Toulouse University Hospital, +12%) and carrying out 1,743 FISH analyses (+11%), resulting in longer delays in reporting results of non-urgent tests.

. The Laboratory's clinical research activity is internationally recognized. It has been identified as a referral center for four treatment protocols; GRALL (adult acute lymphoblastic leukemia), CAALL-FOI (childhood acute lymphoblastic leukemia), FILO (adult acute myeloid leukemia) and IFM (French myeloma network). Moreover, it contributes to numerous registers,

observatories, working groups, national biological collections, as well as various research-specific biological collections.
. The Laboratory is also developing projects in close collaboration with the CRCT teams RNA_{REG} (Dr. S. Manenti) and METAML (Dr. J-E. Sarry). Two of the Laboratory's biologists also lead CRCT teams: Prof. H. Avet-Loiseau (GENIM) and Prof. E. Delabesse (ALTFAL).

SELECTED PUBLICATIONS IN 2020:

. Bories, P. et al. **Impact of TP53 mutations in acute myeloid leukemia patients treated with azacitidine**. PLoS ONE 15, e0238795 (2020).
. Bosc, C. et al. **Autophagy regulates fatty acid availability for oxidative phosphorylation through mitochondria-endoplasmic reticulum contact sites.** Nature Communications 11, 4056 (2020).
. Corre, J. et al. **Del17p without TP53 mutation confers poor prognosis in intensively treated newly diagnosed multiple myeloma patients.** Blood blood.2020008346 (2020)
. Largeaud, L. et al. **Major rise of a chronic lymphoid leukemia clone during the course of COVID-19.** Int J Lab Hematol ijlh.13383 (2020)
. Vergez, F. et al. **CD34+CD38-CD123+ Leukemic Stem Cell Frequency Predicts Outcome in Older Acute Myeloid Leukemia Patients Treated by Intensive Chemotherapy but Not Hypomethylating Agents.** Cancers 12, 1174 (2020).

Pathology Laboratory

Director: Prof. Pierre Brousset
Assistant directors: Prof. Emmanuelle Uro-Coste and Dr. Philippe Rochaix
53,419 cases, including 19,792 external requests
67,050 examinations and 64,109 reports sent to prescribers
440,928 slides read and 194,193 paraffin blocks created, including 43,383 for biopsies
State-of-the-art techniques: virtual histopathology, confocal digital microscopy, multiplex immunolabeling, AI, NGS, mass spectrometry-assisted amyloidosis typing

. The Pathology Laboratory is divided into five units: Conventional Histopathology, Cytology, Immune-histochemistry, Molecular Biology, Digital imaging.
. A member of the INCa-accredited national network of referrals centers (since 2010), it is the regional referral center for four rare cancers: lymphomas – Lymphopath (Prof. P. Brousset); malignant pleural mesotheliomas and rare retroperitoneal tumors – Mesopath (Dr. I. Rouquette); soft tissue and visceral sarcomas – RRePS (Dr. S. Le Guellec); rare neuroendocrine tumors – TENpath (Dr. Marie Danjoux). It is also a national coordinator, alongside Creteil, for the Lymphopath network (12,000 cases per year). The IUCT-O, via its Pathology Laboratory, is, moreover, one of two European referral centers for amyloidosis typing (Dr. M. Colombat).
. Prof. C. Laurent is vice-president of the Scientific Council of the Lymphoma Study Association (LYSA), a French collaborative group of doctors involved in clinical and translational research on lymphomas. Prof. Laurent, in collaboration with Dr. S. Kanoun, is currently coordinating a machine learning project on microscopy and PET-scan images.
In 2020, the APRIORICS project was selected in the Health Data Hub and BPifrance call for papers. Led by Dr. C. Franchet, the study aims to train AI to recognize tumors and their microenvironments from thousands of microscope images of grade II breast cancers. The data (annotated virtual slides) will then be made available to the scientific community under an open-source license. The project, carried out in collaboration with Thales, also benefits from funding by the Toulouse Cancer Laboratory of Excellence (TOUCAN LabEx) and the Foundation for Medical Research (FRM).
. The renewal of the TOUCAN LabEx in 2019 for five years means that it will continue to develop AI through analysis of histological images to predict the characteristics of large B-cell lymphomas (project led by Prof. C. Laurent and Prof. L. Ysabaert).
. Close collaboration with the CRCT makes it possible to develop various projects such as single cell sequencing (scRNA-seq) with the NoLymIT team (leader: Prof. C. Laurent) to evaluate tumor heterogeneity and lymphoid sub-population resistance in tumor microenvironment. A second project works on developing an IT solution for analyzing complex images from functional microscopy (multiplex immunofluorescence) through a machine learning approach with the CRCT team DynAct (leader: Dr. S. Valitutti).
. A further collaboration begun in 2020 with the ARTIOS company resulted in launching an early phase national clinical study led by Prof. F. Dalenc and Dr. J-S. Hoffmann to test the potential of an anti-PolQ molecule in treating breast cancer patients resistant to anti-PARP and presenting BRCA1 mutations.

. Finally, partnerships continue with Illumina to provide a sequencer to test a TSO 500 gene panel for all molecular analysis needs in solid oncology: mutations and therapeutic targets (actionable genes)/gene copies (CMV)/gene translocation and fusion/ mutational loads (to predict immunotherapy responses)/ microsatellite instability. The objective is to determine whether this gene panel could replace the Foundation 1 panel currently used in first-line treatment of lung cancers.

SELECTED PUBLICATIONS IN 2020:

. Congras, A. et al. **ALK-transformed mature T lymphocytes restore early thymus progenitor features**. Journal of Clinical Investigation 10.1172/JCI134990 (2020)

. Laurent, C. et al. **Gene alterations in epigenetic modifiers and JAK-STAT signaling are frequent in breast implant-associated ALCL**. Blood 135, 360–370 (2020).

. Péricart, S. et al. **Exclusive B-cell phenotype of primary prostatic lymphomas: a potential role of chronic prostatitis.** Histopathology 76, 767–773 (2020).

. Prodhomme, M. K. et al. **EMT transcription factor ZEB1 represses the mutagenic POLθ-mediated end-joining pathway in breast cancers.** Cancer Res (2020)

. Quelen, C. et al. **Minimal residual disease monitoring using a 3'ALK universal probe assay in ALK-positive anaplastic large cell lymphoma: ddPCR, an attractive alternative method to real-time quantitative PCR**. J Mol Diagn (2020)

. Rossi, C. et al. **Baseline SUVmax is related to tumor cell proliferation and patient outcome in follicular lymphoma.** haematol 0–0 (2020)

. Syrykh, C. et al. **Accurate diagnosis of lymphoma on whole-slide histopathology images using deep learning.** npj Digital Medicine 3, 63 (2020).

Cancer BioBank (CRB cancer)

Manager: Prof. Anne Gomez-Mascard
270 m² of dedicated space
35 collections
129,310 samples (tumor and non-tumor samples)
6,716 new samples and 12,090 samples provided to research teams

CRB Cancer IUCT
Centre de Ressources Biologiques

. The role of the Cancer BioBank is to facilitate the IUCT-Oncopole's translational and basic research, in line with INCa directives, and help the Institute fulfill its healthcare mission (2018-2022). The year 2020 was marked by both ISO 9001 and NF-S-96 900 certifications, enabling the Cancer BioBank to respond to world class calls for projects, and to participate in a very positive manner —since declared a strong point of the site— in OECI certification (obtained in June 2020) as part of the accreditation process of the IUCT-Oncopole as a Comprehensive Cancer Center.
. Like the two other BioBanks of the Toulouse University Hospital, the Cancer BioBank is certified NF S96-900 (since 2014) and is also a member of the BioMip regional coordination.
. Despite the COVID 19 epidemic, the Cancer BioBank has responded to the demand from researchers and commercial partners and has maintained its overall activity. Actions already undertaken have been continued: creating a "block library" (for the colon, lung, breast and kidney collections) and supplying fresh tissues (in collaboration with the Pathology Laboratory), and annotating the main collections, including the multi-center pancreatic adenocarcinoma collection (INCa-BACAP). Thanks to its reactivity, it has been possible to stock samples of the COROFET collections, a COVID and pregnancy collection, from early April 2020. Il also received the "animal" collection from the Toulouse University Hospital's IHU INSPIRE project and organized the future reception of the HIMIP (hematology) collection, initially stored at Inserm. Other liquid collections (lung, bladder) were also added in 2020.
. The steps to become the CRCT histopathology unit are underway in order to best meet the needs of all on-site researchers.
. Finally, the various collaborations undertaken with industrial partners over the last few years, Laboratoires Pierre Fabre or EVOTEC, continue on with new projects.
. The Cancer BioBank contributed to 55 research projects in 2020, despite the slow-down due to lockdown in the spring of 2020 (28 involving the Institute's partners and 27 with external academic and industrial partners) and 28 clinical studies.
. The year 2020 was also marked by the creation of its own Cancer BioBank logo as well as by the publication of several studies involving the Cancer Biobank.

SELECTED PUBLICATIONS IN 2020:

. Bertin, H., Gomez-Brouchet, A. & Rédini, F. **Osteosarcoma of the jaws: An overview of the pathophysiological mechanisms**. Critical Reviews in Oncology/Hematology 156, 103126 (2020).

. Cavaignac, E. et al. **What Is the Relationship Between the Distal Semimembranosus Tendon and the Medial Meniscus? A Gross and Microscopic Analysis From the SANTI Study Group.** Am J Sports Med 0363546520980007 (2020)

. Frere, C. et al. **Incidence of Venous Thromboembolism in Patients With Newly Diagnosed Pancreatic Cancer and Factors Associated With Outcomes.** Gastroenterology 158, 1346-1358.e4 (2020).
. Karanian, M. et al. **SRF-FOXO1 and SRF-NCOA1 Fusion Genes Delineate a Distinctive Subset of Well-differentiated Rhabdomyosarcoma**: The American Journal of Surgical Pathology 44, 607-616 (2020).

Engineering and Medical Physics Department (DIPM)

Manager: Régis Ferrand
3,049 doses calculated in 2020 (-7.2% compared with 2019)
4,047 doses calculated by the Biomedical Engineering Unit (+46,2% compared with 2019)

. The Engineering and Medical Physics Department (DIPM) consists of a Medical Physics Unit and a Biomedical Engineering Unit. It supports the IUCT-Oncopole's clinical and research activities by installing and maintaining biomedical equipment and by ensuring, via the Medical Physics Unit, that equipment using ionizing radiation, especially imaging and radiation therapy equipment, meets regulatory servicing and operation standards.
. The Medical Physics Unit also contributes to imaging examinations and radiotherapy treatments (patient quality checks, dosimetry for external radiotherapy, brachytherapy and internal radiation therapy) and consolidates collaboration with clinicians from the Radiotherapy Department, carrying out research with the CRCT team RADOPT (leader: Prof. E. Moyal), in which Dr. S. Ken coordinates the "Physics" group. Moreover, in 2020, Dr. L. Simon directed the doctoral dissertation of J. Leste entitled « *Mise en œuvre et apports cliniques d'un modèle Monte-Carlo d'un accélérateur linéaire de radiothérapie externe* » that won the prize of the EAD 23 doctoral school.
. Moreover, since 2018 Dr. S. Ken has been an associate researcher with the MINDS team (coMputational imagINg anD viSion - coordinator: Dr. A. Basarab) of the Toulouse Institute of Computer Research (IRIT) to develop advanced image analysis and interpretation tools. In 2020, Dr. S. Ken joined the "Artificial Intelligence" group of the European Federation of Organisations for Medical Physics (EFOMIP) where he participates, particularly, in organizing a virtual workshop on the need for expertise in AI in medical physics.
. Translational research projects, conducted in collaboration with teams in the "hard sciences", are also ongoing, such as a project in collaboration with medical physics teams from Catalonia and the Institut Sainte Catherine in Avignon to model beams in radiation therapy; collaboration with the Toulouse Institute of Mathematics for the Computreat project (IUCT-Oncopole coordinator: Prof. L. Ysebaert). The Department also contributed to the European Medirad project (dosimetry in vectorized internal radiation therapy, whose IUCT-Oncopole coordinator is Prof. F. Courbon. This project ended in 2020.
. In the context of projects launched in 2019, the Department also collaborates with industrial partners. One such project, in conjunction with General Electric Healthcare (including an "Industrial Contracts for Training through Research" [CIFRE] doctoral project) aims to develop a prototype PET scanner in 2021. The second project, in collaboration with Varian Medical Systems, seeks to perfect a new accelerator by 2022. Collaborations with Oléa Medical or the Toulouse company, JoliBrain, are also ongoing in the field of AI and 4D scanners.
. The Department received a new diagnostic scanner in the Imagery Department and new operating suite imagers and oversaw implementation of the first systems of recognition with body surface positioning.
. The year 2020 was also marked by the installation of a new Halcyon radiotherapy accelerator in the eighth bunker —the latest model Vmat, offering a better quality of on-board imaging in record time (17 s vs 1.5 min most machines on the market). In total, four families of equipment are present on-site: three tomotherapy apparatuses, one of which is "new generation", two LINAC, one Novalis and now, one Halcyon.
. Fundamental concerns were also addressed this year, in collaboration with the radiotherapists, to optimize imagery techniques to identify, from a dosimetric point of view, the most appropriate apparatus for each tumor location. First results of our work on sub-families of breast cancer should be published in early 2021.

Zooming in on AI

Artificial Intelligence (AI) is an expanding field of research touching on a variety of areas and holding enormous potential for the medicine of tomorrow. Consequently, the IUCT-Oncopole, in order to meet various objectives, has launched several projects:

Modeling supervision of patients in home care

Created in partnership with two Toulouse companies, MH-Comm and Alcimed, along with the French national atomic energy research organization, the project led by Prof. J-P. Delord seeks to develop a demonstrator able to very realistically simulate monitoring home care for breast cancer patients.

Improving diagnosis by medical imaging

Dr. S. Kanoun is interested in the perspectives offered by AI for medical imaging and has launched an AI training scheme to recognize tumors from PET images. Thanks to funding from the CALYM (Institut Carnot) consortium, a project to automatically calculate tumor volumes began work in 2020. Dr. S. Kanoun also produced, together with the *Lymphoma Study Association* (LYSA), the Toulouse University Hospital and the Institut Claudius Regaud, an image management tool to securely collect and share medical images used in clinical trials (GaelO). Furthermore, Dr. J. Khalifa, Dr. C. Massabeau and the Department of Medical Physics are, together, exploring the question of improving 4D scan images.

Improving the characterization of tumors on slides

Several projects have been planned within the TOUCAN LabEx 2020-2024 framework (promoter: Prof. P. Brousset):
- Characterizing grade II breast cancers through a non-supervised machine learning approach (the APRIORICS project, led by Dr. C. Franchet).
- Analyzing histological images to predict the characteristics of large B-cell lymphomas (project led by Prof. C. Laurent and Prof. L. Ysabaert).

Moreover, collaboration with the CRCT team DynAct (leader: Dr. S. Valituti) was launched with the Pathology Laboratory's Digital imaging unit to develop an IT solution for analyzing complex images from functional microscopy (multiplex immunofluorescence), also inspired by a machine learning approach.

Supporting decision-making in MDTs

Another project, led by Dr. C. Franchet (OCC Breast Cancer), was awarded funding from the first competitive grant scheme run jointly by the Inter-Ministerial Directorates for Digital Technology (Dinum) and for Public Transformation (DITP). Its first aim is to facilitate decision-making in post-operative MDTs by producing a tool capable of extracting essential medical information from pathology reports and presenting it in an appropriate form. The long-term objective is to reduce administrative work and eliminate and errors in re-transcribing patients' data, but also to enable these data to be used for research purposes.

Gaining precision in Radiotherapy:

The Medical Physics (in particular Dr S. Ken and Dr. L. Simon) and Nuclear Medicine (Dr. S. Kanoun) Departments are also working on AI, in collaboration with Jolibrain, a company specializing in deep learning. One such project aims to create an automatic tissue contouring tool for radiotherapy.

Identifying new biomarkers thanks to radiomics

The Gliomics project, sponsored by Prof. A. Laprie, is using imaging data from the Spectroglio clinical trial to design a radiomics software package to combine radiotherapy data with multimodal MRI data, especially magnetic resonance spectroscopy data. A 2017 grant from the Fondation pour la Recherche Médicale (AAP "Computational Medicine") allows two researchers to work on this project full time, in collaboration with T. Filleron's biostatistics team. The resulting software will also be applied to children's cancers, especially ependymomas. Prof. A. Laprie and Prof. F. Tensaouti have been working on this theme for several years as part of the national PEPPI study. It will be the focus point of a second project entitled EPENDYMOMICS.

APRIORICS

The APRIORICS project – Reinforced Deep Learning through Immunohistochemistry to Requalify Images of Breast Cancer — was selected in the 2020 Health Data Hub call for projects ("Artificial intelligence for improving experience with the healthcare system"). Carried out in partnership with Thales Services, the project also benefits from support by the Foundation for Medical Research (FRM).

EPENDYMOMICS

A Multiomics approach by Deep Learning to Radioresistance of Ependymomas in children and adolescents — was awarded "the Jury's favorite" in the 2020 Unicancer Innovation Competition. The project will aggregate clinical, biological, imaging and radiotherapy data from two consecutive studies having included all children and adolescents with this disease since 2000 in France. It is also laureate of the INCa/DGOS PRTK2020.

Privileged collaborations outside the CRCT

IUT-Oncopole clinicians are members of research laboratories in Toulouse other than the CRCT, allowing them to explore the fight against cancer from complementary approaches.

. Prof. A. Laprie (Radiotherapy Department) is a member of the **DEVIN team (Development and validation of biomarkers in MRI and nuclear medicine/leader: Dr. P. Peran) of the Toulouse Neuro Imaging Center – ToNIC.** This Inserm/University Toulouse III - Paul Sabatier Joint Research Unit 1214 is dedicated to the brain and its main pathologies. The theme under study: brain tumors, ballistics and cognition.

. Prof. C. Vaysse (Surgery Department) is a member of the **Microenvironment cancer and adipocytes** team (leader: Prof. C. Muller) of the Structural Biology and Pharmacology Institute (UMR CNRS 5089 - **IPBS**), focusing in particular on the links between obesity and breast cancer. Since 2017, the team has been working on obesity-induced breast fatty tissue modifications and its role in the aggressiveness of breast cancer.

. Dr. A. Dupret-Bories (Surgery Department) is an associate researcher of the **Interuniversity center for research and materials engineering** (**CIRIMAT** - UMR CNRS INPT UPS 5085/leader: Prof. C. Laurent). Several studies are underway, and collaborations have been set up with companies (Rescoll, AnatomikModeling), to develop innovative products, notably with 3D printing. Dr. A. Dupret-Bories also coordinates the in vivo theme in the TIPOLTI project (Institut Carnot MICA) focusing on developing new osteosynthesis plates to reduce the risk of rejection. In 2020, her BIOFISS project received National Research Agency (ANR) funding; she also participates in an ANR project led by the CIRIMAT center, CongOs.

. Dr. P. Grosclaude and Dr. S. Lamy were seconded to the U1027 Inserm - University Toulouse III-Paul Sabatier **team 5 - EQUITY - Embodiment, social ineQualities, lifecoUrse epidemiology, cancer and chronIc diseases, intervenTions, methodology** (leader: Dr. C. Delpierre). Their work focuses on epidemiological studies on cancers.

. Dr. S. Ken (Engineering and Medical Physics Department) is an associate researcher with the **MINDS team** (**coMputational imagINg anD viSion** – coordinator: Dr. A. Basarab) of the Toulouse Institute of Computer Research (**IRIT**). Its aim is to develop advanced tools for analyzing and interpreting images.

IV

VALORIZATION

Knowledge sharing

185 interns and 65 doctoral students in 2020
11 different student nationalities
14 master's degrees and 9 university and inter-university diplomas associated with the IUCT-Oncopole
68 university educators, numbering 30 professor-hospital practitioners, 25 associate professor-hospital practitioners and ten university hospital assistants.

Strong involvement in university diplomas

Prof. H. Prats is director of the **Master's in Cancerology** at the University of Toulouse III-Paul Sabatier.
Several of our collaborators are also co-directors of university and inter-university diplomas:
. Dr. N. Caunes-Hilary for the university diploma **"Supportive cancer care"**.
. Prof. F. Dalenc for the inter-university diploma **"Breast cancer Oncology: from physiology to after cancer"** (Montpellier, Nîmes, Toulouse).
. Dr. F. Puisset for the university diploma **"Accompanying patients on oral anticancer drugs at the pharmacy"**.
. Drs. L. Balardy and L. Mourey for the inter-university diploma **"Geriatric Oncology"** (Lyon, Toulouse).

A future University Center for Teaching and Research in Healthcare (CUERS)

The University of Toulouse III-Paul Sabatier (UT3) aims to federate all the actors in education and research in biology and healthcare. In this perspective, a building project to host the future unified Faculty of Health Sciences within the context of the University Center for Teaching and Research in Healthcare (CUERS), coordinated by Prof. M. Ayyoub (Vice-President of the UT III Board of Governors), was submitted and has been approved in the State-Region Contract Plan. Two locations are currently being considered to deploy this project. The Oncopole site is one of the options.

The CARe University Research School (EUR)

Within the context of the TOUCAN LabEx renewal, Prof. B. Ségui (CRCT) and Prof. P. Valet (I2MC) have created the Toulouse Graduate School of Cancer Aging and REjuvenation (CARe). Teaching, from first year master's level through doctorate, takes place in English. The main objective is to offer high-level innovative education in cancer, aging and bioengineering, in close relations with pertinent Toulouse research centers. Students are selected from various undergraduate programs – engineering, hard sciences, exact sciences, pharmaceutical and medical studies. From the first year of their master's, students will be constantly immersed in academic or industrial research laboratories. The first cohort of students began the program in 2020.

Continuing success for the Small Private Online Course on care pathways

In 2020, 1,705 students followed the "Care pathways for cancer patients" SPOC offered by the University of Toulouse III-Paul Sabatier, in collaboration with the IUCT-Oncopole. Launched in 2016, this SPOC in now an integral part of initial training for medical and nursing students in Occitanie-Ouest, Brittany and the University of Paris. Continuously evolving, the program will be completed for the beginning of the 2021 academic year with a week-long supplementary course on the specificities of blood cancer care.

European accreditation for surgical training

Through the ICR, the IUCT-Oncopole has been accredited by the European Society of Gynaecological Oncology (ESGO) since 2017 to provide specialized training programs of excellence in gynecological oncology. Only seven other French centers, to date, are accredited for these two-year programs. In 2020, Dr M-A. Angeles is the second IUCT-Oncopole graduate of this "Diploma of European Gynaecological Oncologist".

Continuing training for healthcare professionals

- The IUCT-Oncopole organizes several seminar cycles for researchers and clinicians, as well as regional information and training meetings coordinated by the Onco-Occitanie cancer network.
- At the initiative of COMET, the doctoral students committee of the "PhD Excellence" program, a weekly "Journal Club" was set up for the whole of the IUCT-Oncopole's medical and scientific community.

First birthday of the Oncogeriatrics MOOC: a very positive feedback

Entitled "Cancer in the elderly: understanding its specificities in order to provide better care", this MOOC is a joint venture between Occitanie's two Geriatric Oncology Coordination Units, whose members include the IUCT-Oncopole's Geriatric Oncology OCC. Open to all health professionals, the first two session were broadcast in 2020, followed by 1,794 learners from all across France. The level of overall satisfaction is high (8.5>10)!
mooc-oncogeriatrie.the-mooc-agency.com/

Close collaboration with Oncostream

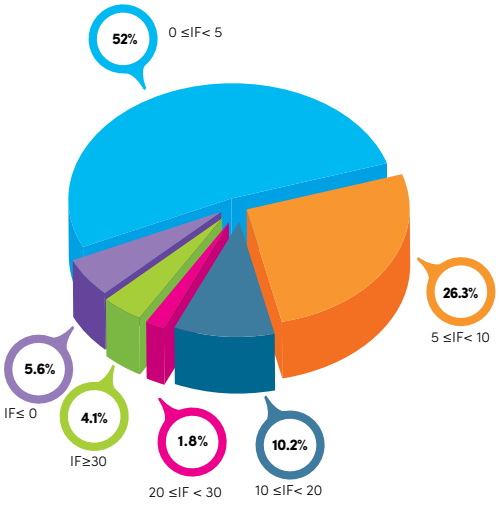
Oncostream is the French Society of Surgical Oncology's (SFCO) Web TV channel. Created in 2014 by Dr G. Ferron (Surgery Department) and L. Vaillat, it can be used to stream, either live or on demand, all types of oncology-related event and training course. It is the largest free platform of its type in France and its use is growing across Europe. Several webinars were produced at the IUCT-Oncopole in 2020.

Training health professionals in non-technical competences: come pilot an Airbus 320!

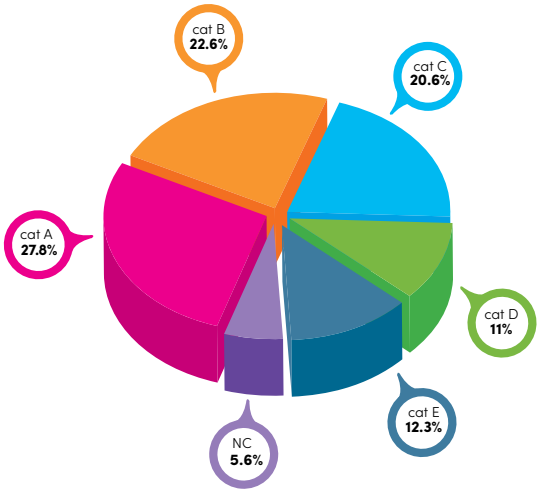
In collaboration with the Quality Department, Dr. R. Fuzier (Anesthesiology Unit) launched an innovative training program in 2020 for physicians and paramedical healthcare professionals called "Is there a care provider in the cockpit?". The day-long program aims to raise participants' awareness of the importance of non-technical competences in their daily work. To do so, an activity was implemented for which none of the participants had any technical competences: piloting an Airbus 320! Only a strategy based on non-technical skills makes it possible to carry out such a mission. Following theoretical training to explain the approach, care provider-learners are then invited to take a seat in the cockpit to apprehend, among other things —and in a completely new manner—, the impact of stress on their performance, teamwork and safety. The sessions are filmed to be discussed later during a common debriefing. To go further, a modular training program (four modules, five days) entitled "Safety culture and human factors in health care" will be available as of September 2021.

Scientific output

The IUCT-Oncopole's basic, translational and clinical research activities gave rise to **782 publications** in 2020 (+24% compared with 2019) in **328 journals** (46% with a SIGAPS A or B ranking).
The mean impact factor (IF, 2019 value, excluding NC*) was **6.87**.



Percentage of 2020 articles by journal impact factor



Percentage of articles by SIGAPS category 2020

International journals in which the IUCT-Oncopole published the most in 2020

1. Cancers
2. Blood
3. European Journal of Cancer
4. Leukemia
5. Journal of Clinical Oncology
6. European Annals of Otorhinolaryngology, Head and Neck Diseases
7. International Journal of Gynecological Cancer
7. The Lancet Oncology
8. British Journal of Haematology
9. World Journal of Urology
10. Haematologica
10. Blood Advances

Moreover, several of the site's clinicians and researchers are long-standing members of editorial boards, notably as **co-editors-in-chief** (**Cancer Chemotherapy and Pharmacology** - Prof. E. Chatelut and Cancers - Prof. C. Laurent), and **associate editors** (**Blood/American Society of Hematology Journal** - Prof. H. Avet-Loiseau, **International Journal of Gynaecological Cancer** - Dr G. Ferron and Dr A. Martinez, **Frontiers in Endocrinology** - Dr C. Bousquet and Dr S. Pyronnet, **Cellular Endocrinology Review** - Dr S. Pyronnet, : **Frontiers in Oncology/Frontiers in Chemistry/ Helyon** - Dr M. Poirot, **Pharmacologia/Frontiers in Nutrition/ Frontiers in Pharmacology** - Dr M. Poirot and Dr S. Silvente-Poirot, **Plos Genetics** - Dr J. Guillermet-Guibert, **International Journal of Molecular Sciences** - Dr A. Lemarié, **American Journal of Cancer Research** - Dr N. Andrieu, **Annales de Dermatologie et de Vénéréologie - Dr V. Sibaud, Médecine Hospitalière** - L. Astudillo).

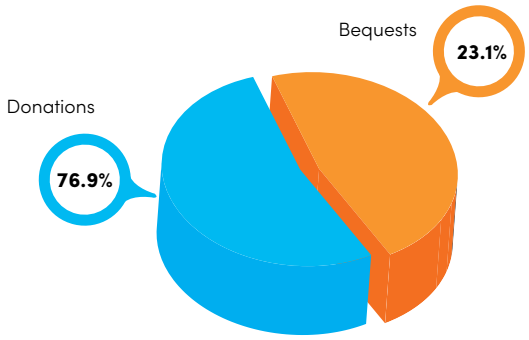
The list of key publications of interest (SIGAPS A ranking and with a 1st, 2nd, penultimate and/or last IUCT-O author) is available in the Appendix at the end of this document.

Support for our work

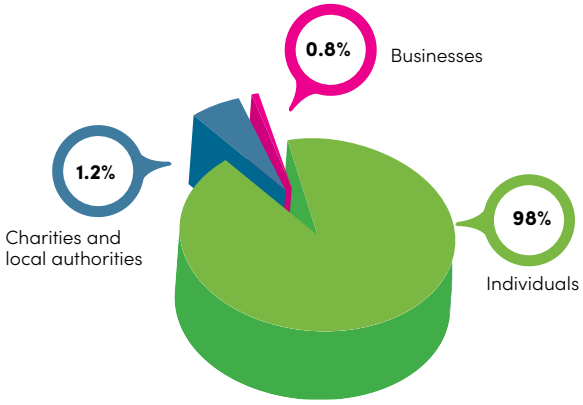
The Covid-19 pandemic marked the year 2020. Numerous private individuals, restaurateurs, business leaders and charities supported the healthcare teams during the first lockdown by generously offering gourmet food or soothing hand lotions.
Local authorities, businesses, charities and especially private individuals, you continued to mobilize at our side in 2020. Thanks to you, we have maintained our innovative activity despite an unprecedented health crisis. New projects to identify and develop innovative therapeutic strategies, as well as to improve the quality of daily life for our patients and their loved ones, have been able to develop.

We would like to express our deepest gratitude to all those who supported us in 2020.

In 2020, 72.61% of the donations and bequests received were allocated directly to the IUCT-Oncopole's research activities (covering 4% of operating costs).



Types of support received in 2020



Origin of donations and bequests received in 2020

In 2020, the Fondation Toulouse Cancer Santé received more than 2,900 donations, and was able to collect more than €958,000 in donations and €903,000 in bequests from companies and individuals from our region*.

*(Non-definitive figures at the time of publication).

Main publications

List of papers published in 2020 in journals ranked SIGAPS A with a 1st, 2nd, penultimate and/or last IUCT-Oncopole author
(highlighted in orange, papers with an impact factor greater than or equal to 10)

1. Aroua, N., Boet, E., Ghisi, M., Nicolau-Travers, M.-L., Saland, E., Gwilliam, R., de Toni, F., Hosseini, M., Mouchel, P.-L., Farge, T., Bosc, C., Stuani, L., Sabatier, M., Mazed, F., Larrue, C., Jarrou, L., Gandarillas, S., Bardotti, M., Picard, M., Syrykh, C., Laurent, C., Gotanegre, M., Bonnefoy, N., Bellvert, F., Portais, J.-C., Nicot, N., Azuaje, F., Kaoma, T., Joffre, C., Tamburini, J., Recher, C., Vergez, F., Sarry, J.-E., 2020. **Extracellular ATP and CD39 activate cAMP-mediated mitochondrial stress response to promote cytarabine resistance in acute myeloid leukemia**. Cancer Discovery CD-19-1008. https://doi.org/10.1158/2159-8290.CD-19-1008

2. Aveline, C., Fuzier, R., Lupescu, R., Choquet, O., members of the i-ALR Association, 2020. **A prospective multicentre observational study on perioperative analgesia practices for total knee arthroplasty in France: the KNEEONE survey.** Br J Anaesth 124, e26–e28. https://doi.org/10.1016/j.bja.2019.11.006

3. Balança, C.-C., Salvioni, A., Scarlata, C.-M., Michelas, M., Martinez-Gomez, C., Gomez-Roca, C., Sarradin, V., Tosolini, M., Valle, C., Pont, F., Ferron, G., Gladieff, L., Vergez, S., Dupret-Bories, A., Mery, E., Rochaix, P., Fournié, J.-J., Delord, J.-P., Devaud, C., Martinez, A., Ayyoub, M., 2020. **PD-1 blockade restores helper activity of tumor-infiltrating exhausted PD-1hiCD39+ CD4 T cells.** JCI Insight. https://doi.org/10.1172/jci.insight.142513

4. Bálint, š., Müller, S., Fischer, R., Kessler, B.M., Harkiolaki, M., Valitutti, S., Dustin, M.L., 2020. **Supramolecular attack particles are autonomous killing entities released from cytotoxic T cells**. Science 368, 897–901. https://doi.org/10.1126/science.aay9207

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6. Becq, A., Camus, M., Arrivé, L., Hor, T., Amoodadashi, D., Buscail, L., Chaput, U., 2020. **IgG4-related sclerosing cholangitis presenting as an isolated intrahepatic stenosis: a rare presentation of a rare disease**. Endoscopy a-1244-9065. https://doi.org/10.1055/a-1244-9065

7. Bery, N., Miller, A., Rabbitts, T., 2020. **A potent KRAS macromolecule degrader specifically targeting tumours with mutant KRAS**. Nat Commun 11, 3233. https://doi.org/10.1038/s41467-020-17022-w

8. Bosc, C., Broin, N., Fanjul, M., Saland, E., Farge, T., Courdy, C., Batut, A., Masoud, R., Larrue, C., Skuli, S., Espagnolle, N., Pagès, J.-C., Carrier, A., Bost, F., Bertrand-Michel, J., Tamburini, J., Récher, C., Bertoli, S., Mansat-De Mas, V., Manenti, S., Sarry, J.-E., Joffre, C., 2020. Autophagy regulates fatty acid availability for oxidative phosphorylation through mitochondria-endoplasmic reticulum contact sites. Nature Communications 11, 4056. https://doi.org/10.1038/s41467-020-17882-2

9. Braun, M., Aguilera, A.R., Sundarrajan, A., Corvino, D., Stannard, K., Krumeich, S., Das, I., Lima, L.G., Meza Guzman, L.G., Li, K., Li, R., Salim, N., Jorge, M.V., Ham, S., Kelly, G., Vari, F., Lepletier, A., Raghavendra, A., Pearson, S., Madore, J., Jacquelin, S., Effern, M., Quine, B., Koufariotis, L.T., Casey, M., Nakamura, K., Seo, E.Y., Hölzel, M., Geyer, M., Kristiansen, G., Taheri, T., Ahern, E., Hughes, B.G.M., Wilmott, J.S., Long, G.V., Scolyer, R.A., Batstone, M.D., Landsberg, J., Dietrich, D., Pop, O.T., Flatz, L., Dougall, W.C., Veillette, A., Nicholson, S.E., Möller, A., Johnston, R.J., Martinet, L., Smyth, M.J. & Bald, T., 2020. CD155 on Tumor Cells Drives Resistance to Immunotherapy by Inducing the Degradation of the Activating Receptor CD226 in CD8+ T Cells. Immunity 53, 805-823.e15. https://doi.org/10.1016/j.immuni.2020.09.010

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11. Cavaignac, E., Sylvie, R., Teulières, M., Fernandez, A., Frosch, K.-H., Gomez-Brouchet, A., Sonnery-Cottet, B., 2020. **What Is the Relationship Between the Distal Semimembranosus Tendon and the Medial Meniscus? A Gross and Microscopic Analysis From the SANTI Study Group**. Am J Sports Med 036354652098007. https://doi.org/10.1177/0363546520980076

12. Chari, A., Samur, M.K., Martinez-Lopez, J., Cook, G., Biran, N., Yong, K.L., Hungria, V.T. de M., Engelhardt, M., Gay, F., Garcia-Feria, A., Oliva, S., Oostvogels, R., Gozzetti, A., Rosenbaum, C.A., Kumar, S.K., Stadtmauer, E., Einsele, H., Beksac, M., Weisel, K.C., Anderson, K.C., Mateos, M.-V., Moreau, P., San Miguel, J., Munshi, N.C., Avet-Loiseau, H., 2020. **Clinical Features Associated with COVID-19 Outcome in MM: First Results from International Myeloma Society Dataset.** Blood blood.2020008150. https://doi.org/10.1182/blood.2020008150

13. Chauvin, M., Borys, D., Botta, F., Bzowski, P., Dabin, J., Denis-Bacelar, A.M., Desbrée, A., Falzone, N., Lee, B.Q., Mairiani, A., Malaroda, A., Mathieu, G., McKay, E., Mora-Ramirez, E., Robinson, A.P., Sarrut, D., Struelens, L., Vergara Gil, A., Bardiès, M., 2020. **OpenDose: open access resources for nuclear medicine dosimetry.** J. Nucl. Med. https://doi.org/10.2967/jnumed.119.240366

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