ACTIVITY REPORT

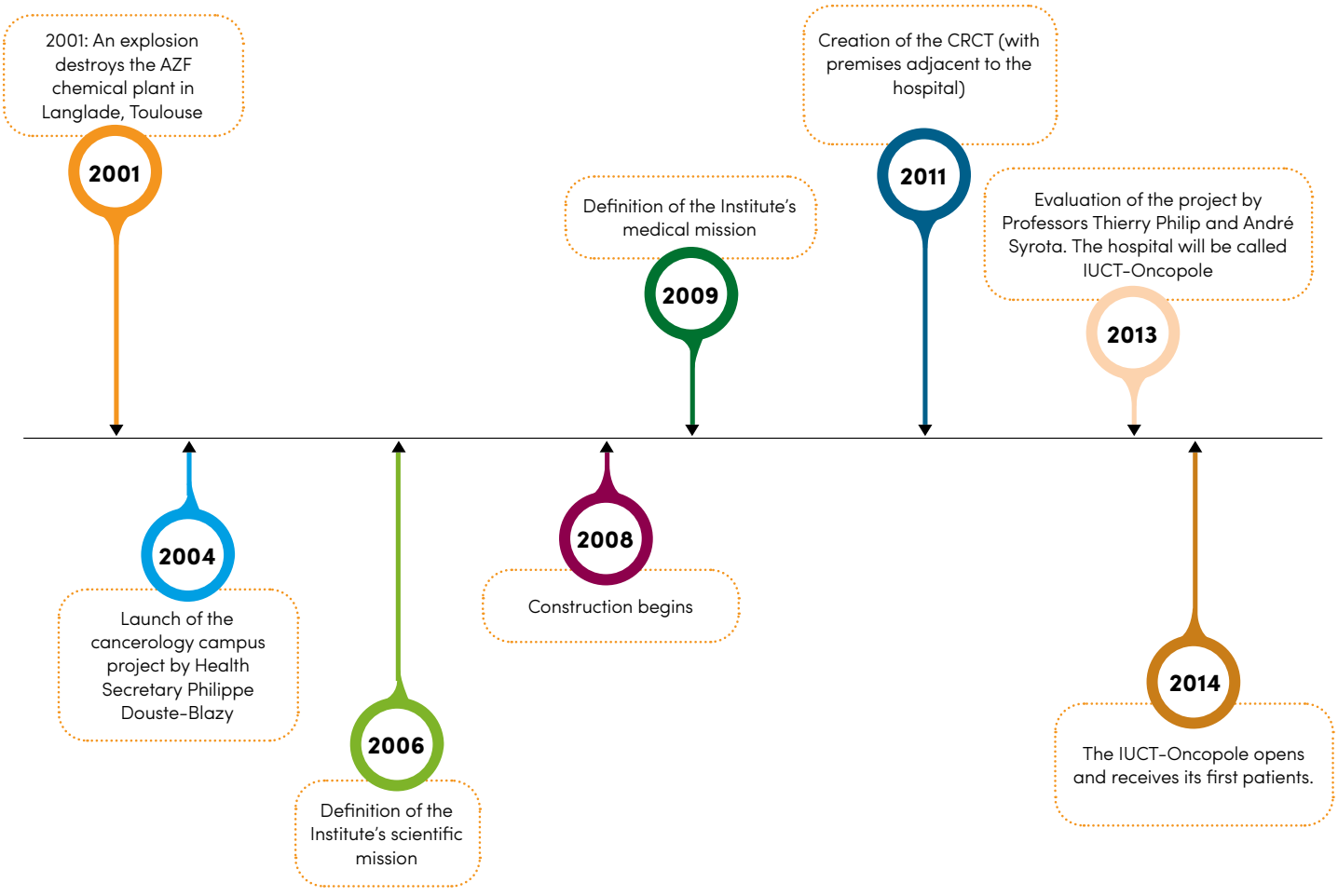
TOULOUSE UNIVERSITY CANCER INSTITUTE-ONCOPOLE

—

2019

INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
Oncopole

Milestones in the construction of the IUCT-Oncopole



The IUCT-Oncopole (Toulouse University Cancer Institute-Oncopole) is a specialist cancer care and research center that was formed by bringing together on a single-site Toulouse University Hospital's oncology departments and activities, the Institut Claudius Regaud (cancer care and research center) and the Cancer Research Center of Toulouse (CRCT). This model, which is unique in France, has produced a cluster of expertise and cutting-edge facilities that enables 1,900 healthcare professionals to provide the highest standards of cancer care, research and teaching.

Patient numbers have increased every year since the IUCT-Oncopole opened in 2014, allowing more than 1,700 people to benefit from innovative therapies in 2019. In addition, the institute is currently running 450 clinical trials, a third of which are devoted to immunotherapy. 56% of inclusions are for early-phase trials. The presence of numerous clinicians within the CRCT's 21 basic and translational research teams has proved to be a powerful driver of innovation all along the treatment-research continuum.

This report presents the results achieved by the IUCT-Oncopole in 2019, including oncology activities in Purpan and Rangueil-Larrey sites.

Contents

Publication managers: Pr Jean-Pierre Delord, Pr Gilles Favre, Jean-Marc Perez. **Editorial committee**: Anne-Laure Fize, Valérie Flipo, Dominique Lautier, Alexandre Abgrall. **Photos credits and graphics**: Laurent Mazoyer, Hélène Ressayres, Ligne Sud, CHU de Toulouse, Igor Bertrand (CHU Toulouse), P.Nin (CRCT). **Design and production**: Agence Ligne Sud. **Translation**: Paul Henderson. **Printing**: Evoluprint

KEY FIGURES 2019

1,900 staff
166 physicians
163 researchers
1,246 students

10,555 new patients (active files)
35,423 patients treated

107,899 hospital stays
Mean length of stay for full hospitalization: **6.20 days**
79.6% outpatients in hospital departments
306 beds - **94** day-hospital beds
58,107 radiotherapy sessions

187 transplants and **8** patients treated with *CAR-T cells*
11 technical support centers
201 clinical studies included patients in 2019
16% of patients (active files) included in a clinical trial
633 publications
16 new patents
Less than 6 months for a CRCT discovery to be translated into a clinical trial at the IUCT-O

€764,643
in donations and bequests
15,000 donors
1 foundation

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

“Consolidation and excellence”

In 2019, Professor Michel Attal stepped down from his role as General Manager of the Institut Claudius Regaud and Administrator of the IUCT-Oncopole. Professor Attal’s leadership helped create the constructive partnership with Toulouse University Hospital that gave the IUCT-Oncople its initial impetus. In addition, the dynamism he instilled enabled the IUCT-Oncopole to achieve its founding objectives: become a regional referral center; provide the highest quality care and innovative therapies to patients, especially those with complex pathologies; make the IUCT-Oncopole’s expertise available to all of the region’s public healthcare facilities; construct fruitful collaborations with the Cancer Research Center of Toulouse and turn it into one of Europe’s leading centers for clinical and translational research.

This initial project has now entered the consolidation phase, during which we must continue pursuing the IUCT-Oncopole’s mission and maintain the mindset with which we have worked for the last six years. We must live up to the standards of excellence achieved in patient care, in medical innovation and, most fundamentally, in scientific research.

To achieve this, we must continue adapting our healthcare offer to patients’ needs, especially in the field of hematology. In terms of innovation and clinical research, we must do more to promote entirely new approaches in areas such as identifying molecular signatures, predicting the risks and effects of treatments, and detecting and measuring “residual diseases”. Intensifying our efforts in basic research fields (e.g., single-cell studies of cancer cell metabolism) will require strong support from the technical centers that serve both our clinical and research activities. Indeed, by integrating input from the hard sciences, especially mathematics, 21st-century medicine now has the capacity to process the massive and complex datasets generated by healthcare and research projects.

With consolidation and excellence as our watchwords, our roadmap for the years to come is clear: the only way to improve the effectiveness of the treatments we offer patients is to ensure the IUCT-Oncopole’s clinical and translational research is on a par with that produced by the world’s leading research centers. We are determined to build on the legacy left by Professor Attal, whom I have succeeded, aware of the responsibility that falls on my shoulders. This legacy is part of Toulouse University Hospital’s and the Institut Claudius Regaud’s heritage, and it impels us to strive for excellence.

“IUCT-O, innovation in oncology”

Marc Penaud, General Manager of Toulouse University Hospital

For the last six years, Toulouse University Cancer Institute-Oncopole (IUCT-O) has combined the strengths of Toulouse University Hospital and the Institut Claudius Regaud to create a force for advancing cancer research, treatment, and training that is unique in France. By making innovation the core of its activities, it is already able to offer the region’s cancer patients the therapies of the future.

Medical innovation at the heart of the healthcare offer. In 2019, the Hematology Department, under Professor Recher, introduced personalized immunotherapy to Toulouse when it began offering patients CAR-T cell (Chimeric Antigen Receptor T-cell) therapy. This highly promising gene therapy gives hope to innumerable patients with what were once considered incurable lymphomas. Although CAR-T cell therapy is still in its early days at the IUCT-O, our departments are already investigating new indications for leukemia and conducting clinical trials on certain myelomas. In time, around 60 patients will be able to benefit from this highly personalized therapy every year.
The IUCT-O’s innovative work in cancerology affects all aspects of public-sector cancer treatment in the Toulouse area. For example, surgeons at Toulouse University Hospital recently performed the world’s first nose reconstruction on a patient suffering from five basal cell carcinomas.

Innovation in the quality of treatment and research. After more than 18 months’ preparation and an unprecedented commitment from all of our teams, the Organisation of European Cancer Institutes (OECI) has granted the IUCT-Oncopole “Comprehensive Cancer Center” certification. This accreditation, awarded following a successful onsite audit, admits the IUCT-Oncopole into the very exclusive circle of Europe’s leading cancer treatment, research, and innovation centers.

The next step in our continuous improvement dynamic is to achieve recognition for the quality of cancer care and the fluidity of patient pathways across all of Toulouse’s public-sector cancer treatment centers by obtaining OECI “Cancer Network” accreditation. The cancer care departments at the IUCT-O and at Toulouse University Hospital’s Purpan, Rangueil, and Larrey sites, grouped together as the Toulouse Association for Public-Sector Oncology (ATOP), are fully committed to becoming the first such network to be certified in Europe. In parallel, the European Neuroendocrine Tumor Society (ENETS) has certified Toulouse University Hospital and the IUCT-O as a “European Center of Excellence for Neuroendocrine Tumors”, thereby providing international recognition for our multidisciplinary expertise in caring for patients with digestive neuroendocrine tumors.

Organizational innovation. Ensuring excellence, quality, and innovation requires adept governance and flexible management. As of 2020, this role will soon be filled by the Public-sector Hospital-University Oncology Federation. The new body, chaired by Professor Julien Mazières, will define a united strategy and ambitious medical-scientific objectives for all of Toulouse University Hospital’s cancer care and research units at the IUCT-O, Purpan, Rangueil, and Larrey.
I would like to end by saluting the work accomplished by Professor Michel Attal, without whom the IUCT-O would not be the center it is today, and by expressing my complete confidence in Professor Jean-Pierre Delord. Together, we will ensure this unique cancer treatment and research initiative continues its exemplary work in the service of patients.
Finally, I would like to thank every member of staff for their unceasing efforts to help drive back cancer and care for our patients. This activity report is a testament to their hard work.

Consolidation of its research themes, renewal of the LabEx TOUCAN, creation of the CARE University Research School — the CRCT, guided by its director, Professor Gilles Favre, is raising its sights and showing its commitment to openness.

Prof. Gilles Favre

“Strengthen our commitment to openness”

What were the events that shaped 2019?
2019 was an opportunity to review our objectives for the next few years, to restructure our research teams and to ask ourselves the questions that will give us a clearer picture of the years to come. Every five years, the High Council for Evaluating Research and Higher Education (Hcéres) assesses the CRCT's teams before deciding on their renewal. Our researchers worked hard to prepare this audit, which took place in November.

What are the CRCT's main research themes?
The CRCT's research activities are structured around four themes (Oncogenic signaling, DNA damage and genetic instability; RNA and cancer; Tumor microenvironment and metabolism; and Oncoimmunology), which are the focus of 17 teams, that is, 420 people. Added to this are two integrated research programs (Therapeutic resistance and Development of mathematical, physical and computing approaches in oncology), conducted in partnership with the IUCT and other research teams in Toulouse. The renewal of the TOUCAN "Laboratory of Excellence" in 2019, with €3 million in funding over five years, has consolidated the resistance mechanisms in hematological cancers research program.

What is the CRCT's goal for the next few years?
Step up a level every year. Raise the CRCT's profile and increase its international recognition. Research should never plateau, it must continue to grow, always aim higher. At the CRCT, this goal is combined with a strong commitment to openness. The center houses researchers from the Laboratory for the Analysis and Architecture of Systems (LAAS-CNRS) and, soon, from Toulouse Institute of Computer Science Research (IRIT), who will work on programs involving massive datasets and artificial intelligence. Toulouse is unusual in this respect, as we are one of the few centers to incorporate researchers from other disciplines. It also clearly shows the direction we are heading: towards the convergence of the hard sciences and our biological and medical sciences.
In collaboration with our colleagues in the field of aging, we are sponsors of the CARE (Cancer, Aging and Rejuvenation) project, which was awarded a University Research School (EUR) grant. This project will be used to train master's and doctoral students, most notably in new specialties incorporating mathematics and computing.
Further examples of our commitment to openness include the continuing collaboration with Roche/Genentech (the IUCT-Oncopole is one of 20 Roche/Genentech global immunotherapy centers of excellence) on ambitious projects that bring together three CRCT research teams and clinical teams from the IUCT; the growing number of papers we publish, often in high-impact journals and increasingly written jointly by a researcher and a clinician; and the creation of startups arising from the Center's projects.

What is next for the CRCT?
We are currently working on an application for state-region development funding (Contrat de Plan État-Région). We hope to enhance our technological capabilities, especially with respect to very high throughput sequencing, so we can continue raising the level of our research, which we would like to orient more-and-more toward single-cell studies.

The High Council for Evaluating Research and Higher Education (Hcéres) has extended its evaluation mission to research carried out in university hospitals. Professors Camille Laurent and Julien Mazières coordinate cancer research at Toulouse University Hospital.

Prof. Camille Laurent and Julien Mazières

“Encourage transversal projects”

What was the background to this evaluation?

Julien Mazières : Hcéres now assesses university hospitals as research establishments. Hence, the evaluation carried out in December 2019 focused exclusively on the university hospital and concerned research conducted between 2014 and 2019.

Camille Laurent : The dossier presented by the university hospital contained several predetermined themes: aging, neurology, cardiology, new technologies and cancer. The assessment included research training, as well as research activities and innovation.

Which points did the evaluation focus on?

Julien Mazières : The first part looked at whaaat we have done over the last few years. This enabled us to explain how cancer research in Toulouse is structured, highlighting five key aspects: the restructuring of public-sector cancer research and treatment in the Toulouse area since 2014; the coordination of phase III trials, which has impacted patient care; the organization of translational research with the CRCT, especially through Labex Toucan; the development, unique in France, of epidemiological and social pharmacology within the Captor project; and the constitution of patient cohorts and biobanks.

Camille Laurent : For example, we are scientific managers for the CALYM Carnot Institute-sponsored CeVI viable-cell collection, which brings together more than 6,000 annotated lymphoma samples collected by six centers in France. The Toulouse team also coordinates the international myeloma cohort, the largest such collection in the world, and the BACAP cohort of pancreatic cancer samples, promoted by Toulouse University Hospital, which is unique in France.

In addition, Toulouse has a worldwide reputation for the quality of its cancer research: we are members of influential collaborative groups; we have many international experts; we have been awarded scientific honors; and we benefit from the reputation of our most influential researchers, most notably Professors Michel Attal and Hervé Avet-Loiseau.

What does the future hold?

Julien Mazières : From an organizational point of view, our objective is to make Toulouse a unique public-sector cancer research and treatment project, certified by a European quality label (OECI certification). In terms of our research themes, we are looking to develop both translational research and transversal projects. Thus, each theme, organ by organ, will continue making advances in translational research, databases, the biobank and clinical trials, while also promoting more ambitious transversal projects that will further strengthen Toulouse’s reputation. The three themes we wish to pursue are early evaluation of cancer risks, optimization of existing treatments, and characterization of resistance mechanisms.

Camille Laurent : A final theme — using new technologies and artificial intelligence to benefit patients — is also a top priority.

Cancer research in numbers

1,000 papers in five years
800 clinical trials
5,000 patients included

HIGHLIGHTS OF 2019

JANUARY

Launch of "Mon E-Suivi IUCT-Oncopole"

This smartphone app completes the range of telephone-based systems to monitor patients at home.

FEBRUARY

LabEx TOUCAN renewed for five years

The TOUCAN (LabEx 2011) "Integrated Analysis of Resistance in Hematological Cancers" project led by Prof. P. Brousset is extended for five years (€8.5 millions).

MARCH

CLIP2 accreditation renewed

INCa renews the Clinical Trials Bureau's accreditation as a CLIP^2 early-phase trials center (coordinator: Prof. J-P. Delord) for five years.

APRIL

In red & black

Stade Toulousain rugby club uses its match against AS Clermont Auvergne to put the spotlight on the Sport & Cancer initiative, a partnership between the IUCT-Oncopole, Stade Toulousain, CAMI and Malakoff Médéric Humanis.

MAY

580,000 euros for the SI2GMA project

SI2GMA, a project led by Prof. E. Moyal, is awarded funding under the Fondation ARC's first SIGN'IT competitive grants scheme. SI2GMA is designed to study the effectiveness of combining radiotherapy with immunotherapy in treating recurrent glioblastoma.

JUNE

42 presentations at the ASCO Annual Meeting

The IUCT-Oncopole and the CRCT give a total of 42 presentations at the 55th Annual Meeting of the American Society of Clinical Oncology. They include an oral presentation by Prof. M. Attal, in conjunction with P. G. Richardson of the Dana Farber Cancer Institute.

JULY

CAR-T cells at the IUCT-Oncopole

The first patient receives CAR-T cell therapy at the IUCT-Oncopole on July 30, 2019. A further seven patients benefit from this innovative form of immunotherapy between September and December 2019.

AUGUST

Le Point rankings of hospital and clinics

In Le Point magazine's 2019 rankings, the IUCT-Oncopole is placed 3rd for treating head and neck cancer, 5th for breast cancer surgery and 6th for gynecological cancer surgery.

SEPTEMBER

Accredited "European Centre of Excellence for Neuroendocrine Tumors"

The European Neuroendocrine Tumor Society (ENETS) certifies the joint IUCT-Oncopole and IUCT-Rangueil/Larrey as a "University Centre of Excellence for Neuroendocrine Tumors".

OCTOBER

Dermatological toxicities: launch of a European network

Dr V. Sibaud, in collaboration with Naples University Hospital and Madrid University Hospital, launches the "European Network for Cutaneous Adverse Events to Oncologic Drugs" (ENCADO).

The IUCT-Oncopole lit up in pink

The building's façade is lit up in pink for the "Pink October" cancer awareness week. More than 300 patients attend the presentations and workshops held during the 4th La Vie Après ("Life After") open day.

NOVEMBER

"Highly Cited Researchers 2019"

Clarivate Analytics names Prof. H. Avet-Loiseau as one of the most influential researchers of the last decade.

The IUCT-Oncopole becomes a tobacco-free area

The IUCT-Oncopole takes advantage of "No Tobacco Month" to sign a "Tobacco-free Area" agreement with the Ligue Contre le Cancer and thereby become the Haute-Garonne département's first tobacco-free site.

Evaluation of the CRCT

The High Council for Evaluating Research and Higher Education (Hcéres) audits the CRCT's teams as part of the center's renewal process.

DECEMBER

"Alliance Oncopole"

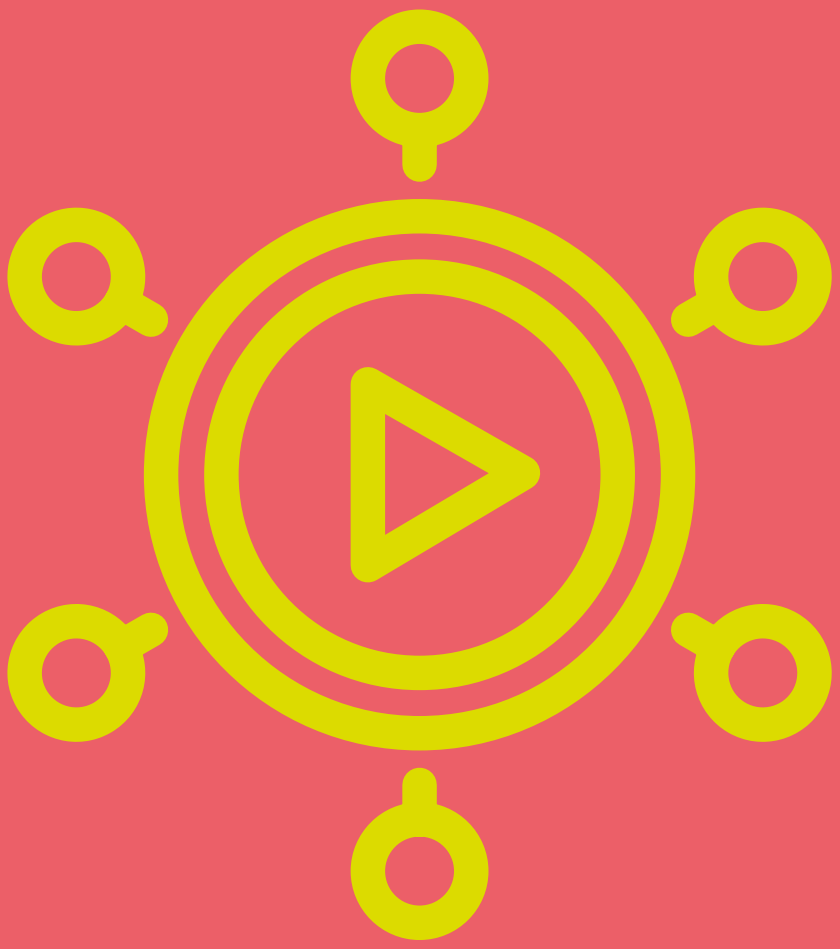
A multi-annual agreement is signed with the Pierre Fabre Research Institute in order to boost innovation in cancerology and develop new personalized therapies.

OECI accreditation visit

Auditors from the Organisation of European Cancer Institutes assess the site as part of the Comprehensive Cancer Center accreditation process.

The IUCT-Oncopole at the San Antonio Breast Cancer Symposium (SABCS)

Members of the IUCT-Oncopole give ten presentations, including a plenary lecture by Prof. Florence Dalenc (results of the SAFIR02-IMMUNO phase II clinical trial - promotion UNICANCER).



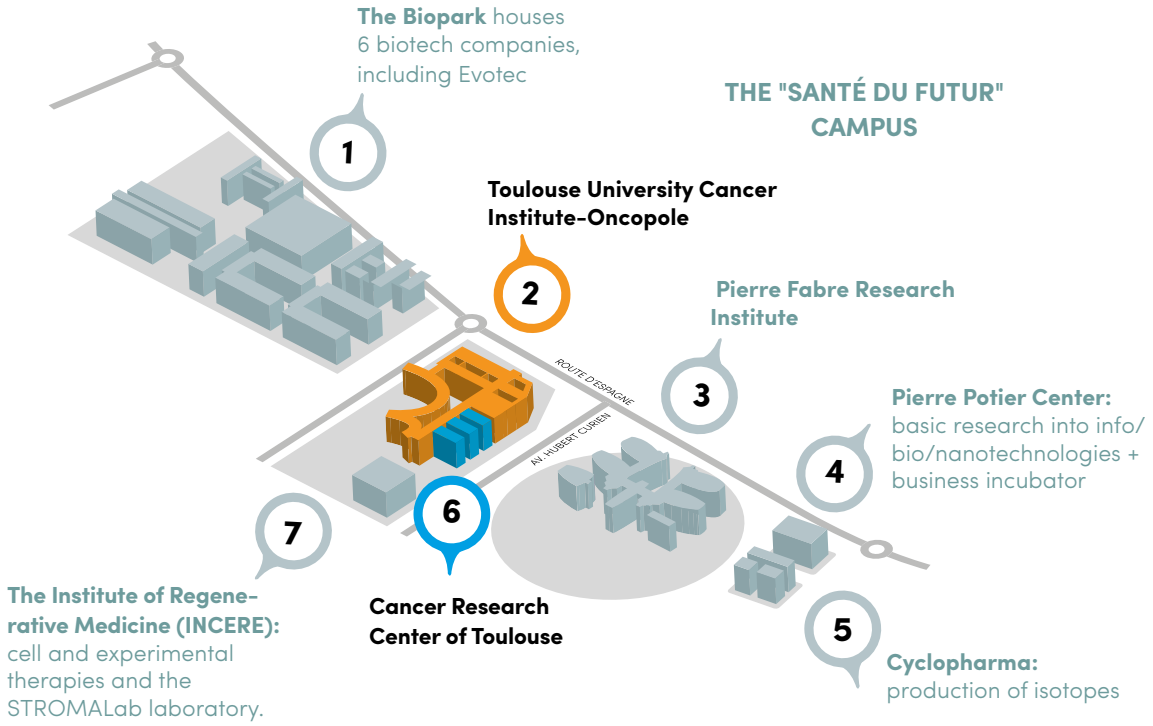
1

A REFERENCE CENTER AT THE HEART OF NETWORKS

A single site

The "Santé du Futur" Campus

"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.



A Biopark houses the Sanofi chemistry bank, technical support centers (*Trans-Hub Integrated Sanofi Platform, exploratory unit, in vivo and in vitro screening*), and six biotech companies (EVOTEC, DExStr, Hyphen, Lifesearch, Omilo, TIST).

The Advanced Technology Institute in Life Sciences (ITAV)/Pierre Potier Center contains a research center with seven CNRS research teams, a bio-nanotechnology unit, an automated chemical synthesis unit, a photonic multi-scale imaging unit, and a business incubator.

The Institute of Regenerative Medicine (INCERE) is a coalition of public and private research teams, managed by the Occitanie Pyrénées-Méditerranée branch of the French Blood Service. INCERE's 3,000-m2 premises house the STROMALab laboratory, which comprises teams from the French Blood Service, the University of Toulouse III-Paul Sabatier, Toulouse National Veterinary School (ENVT), the CNRS and Inserm. INCERE also houses a number of stem-cell start-ups, including Cell-Easy, which joined the unit in April 2019 and provides access to state-of-the-art production equipment.

A Community Center close to the IUCT-Oncopole offers a wide range of patient services, including *the départemental* branch of the Ligue Contre le Cancer, a specialist hairdressing salon, and adapted physical activities, etc.

Finally, 2019 saw the opening of the Estela **cancer and geriatric aftercare and rehabilitation clinic**. In order to guarantee continuity of treatment for cancer patients, the IUCT-Oncopole has signed a partnership agreement with Estela to provide training for the clinic's medical and paramedical staff.

Reception Hall

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**
with 9 technical services units (manager: F. Lopez)

• **A Preclinical Trials Center**
CREFRE-US006 (directors: Dr Y. Barreira, then Dr M. Bardotti)

• **A Pathology Laboratory**
with 30 practitioners (manager: Prof. P. Brousset)

• **An Onco-Hematology Transfer Platform**
with 2 research units focusing on myeloma genomics (manager: Prof. H. Avet-Loiseau) and acute leukemia (manager: Prof. E. Delabesse)

• **An Oncology Medical Biology Laboratory**
(manager: Prof. G. Favre) with 5 units: Pharmacology (manager: Prof. E. Chatelut), Rapid Response Biology (manager: Dr L. Malard), Exploratory Biology (manager: Dr A. Pradines), Oncogenetics and Pharmacogenetics (manager: Dr C. Toulas), and Immunity Monitoring (manager: Prof. M. Ayyoub).

• **A Cancer BioBank Center**
(CRB) (manager: Prof. A. Gomez-Brouchet)

• **A Biopathology Clinical Trials Support Unit**
(SBEC) (manager: Prof. P. Rochaix)

• **A Pharmaceutical Clinical Research Unit**
(manager: Dr A. Grand)

Sustainable development at the IUCT-Oncopole

The "Santé du Futur" campus was built on brownfield land and is gradually being incorporated into Toulouse Metropolitan Council's sustainable development dynamic. A 2.5-km greenway beside the Garonne River, between the campus and the Prairie des Filtres, provides a traffic-free route to the city center for pedestrians and cyclists, while the new Urbain Sud cable car will whisk passengers from the Oncopole to Rangueil University Hospital and then the University of Toulouse III–Paul Sabatier (3 km) in just 10 minutes. Due to open at the end of 2020, it will be France's largest urban cable car. The campus' own solar power plant should also be completed by the end of 2020. Built with support from the Ministry for Environmental Transition and Solidarity's Energy Regulation Commission, 35,000 solar panels, covering an area of 19 hectares, will produce around 3 million kWh per year - enough electricity to meet the needs of 3,000 people.
Initiatives taken by the IUCT-Oncopole itself include using eco-grazing to maintain the campus's lawns (six Castillonnaise sheep have grazed on 3,000 m^2 of grass since 2017) and installing beehives on the building's roofs (they produce between 30 and 50 kg of honey per year).

Structure

A Strategy Council, a joint Scientific Directorate for care and research center, and a Scientific Advisory Board work in concert to oversee the site's governance. All translational research programs are steered jointly by a physician and a researcher.

The three IUCTs: Oncopole, Purpan, Rangueil/Larrey

The Institut Claudius Regaud (ICR) and Toulouse University Hospital's oncology departments have combined their strengths to provide comprehensive and innovative public-sector cancer care across the entire Toulouse area. The different specialties are divided, with no overlap, between three sites: IUCT-Oncopole, IUCT-Purpan and IUCT-Rangueil/Larrey.

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 (split-site department)
- Radiotherapy
- Nuclear medicine and brachytherapy

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE
Purpan

- Bone cancers
- Cancers of the nervous system
- Geriatric oncology (split-site department)
- Pediatric oncology
- 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

The IUCT-Oncopole GCS and its Strategy Council

The IUCT-Oncopole GCS is a healthcare consortium (Groupement de Coopération Sanitaire) set up under private law and with the Institut Claudius Regaud and Toulouse University Hospital as equal partners.
Its operations are governed by a set of internal regulations that define each establishment's legal responsibilities, authority and tasks. Most consultative bodies are joint Toulouse University Hospital–Institut Claudius Regaud structures and operate within the frameworks allowed by each establishment's statutes and rules.
Joint governance mechanisms have been in operation since the IUCT-Oncopole opened.

GLOSSARY OF FREQUENTLY USED TERMS

• **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 Toulouse University Hospital.
• **The three IUCTs:** since the Institut Claudius Regaud joined forces with Toulouse University Hospital's cancer departments, cancer care in the Toulouse area has been shared between three sites: IUCT-Oncopole, IUCT-Purpan and IUCT-Rangueil/Larrey. Together, they provide a comprehensive public-sector cancer care service, with each site specializing in different types of cancer with no overlap between specialties.
• **IUCT:** a public interest group (Groupement d'Intérêt Public – GIP) comprising all the area's cancer treatment, research and training establishments, together with Toulouse Metropolitan Council, the Oncomip network (now Onco-Occitanie), the Ligue Contre le Cancer and the Fondation Toulouse Cancer Santé.

Care provided through Organ Coordination Committees (OCCs)

Patient care at the IUCT-Oncopole is the responsibility of Organ Coordination Committees (OCCs), which establish the most appropriate integrated care pathway for each patient, depending on his/her pathology. The specialists involved in determining patient pathways meet every week.

List of the IUCT-Oncopole's 15 OCCs:

Breast Cancer OCC
Coordinators: Prof. Florence Dalenc – Dr Eva Jouve – Dr Charlotte Vaysse

Gynecological Cancers OCC
Coordinators: Dr Laurence Gladieff

Head and Neck Cancers OCC
Coordinators: Prof. Sébastien Vergez – Dr Michel Rives

Sarcomas OCC
Coordinator: Dr Christine Chevreau

Neuro-oncology OCC
Coordinators: Prof. Elizabeth Moyal – Dr Delphine Larrieu-Cirron

Skin Cancers OCC
Coordinators: Prof. Nicolas Meyer – Dr Dimitri Gangloff

Urologic Cancers OCC
Coordinators: Prof. Bernard Malavaud – Dr Loïc Mourey – Dr Pierre Graff-Cailleaud

Oncogenetics OCC
Coordinator: Prof. Rosine Guimbaud

Geriatric Oncology OCC
Coordinators: Dr Loïc Mourey – Dr Laurent Balardy

Supportive Care OCC
Coordinators: Dr Nathalie Caunes-Hilary – Dr Virginie Woisard

Hematology OCC
Coordinators: Prof. Christian Récher

Thyroid and Neuroendocrine Cancers OCC
Coordinators: Prof. Frédéric Courbon – Prof. Rosine Guimbaud – Prof. Delphine Vezzosi.

Thoracic Cancers OCC
Coordinator: Prof. Julien Mazières

Digestive Cancers OCC
Coordinator: Prof. Rosine Guimbaud

Pediatric Oncology OCC
Coordinators: Prof. Anne Laprie – Dr Marie-Pierre Castex

MEMBERS OF THE EXECUTIVE COUNCIL IN 2019

The IUCT-Oncopole GCS

President: Marc PENAUD, General Manager of Toulouse University Hospital
General Assembly

Administrator: Prof. Michel ATTAL, General Manager of the IUCT-Oncopole
Administrative Directors:
Jean-Marc PEREZ
Elvis CORDIER

Executive Council
. Prof. Michel Attal
. Prof. Odile Beyne-Rauzy
. Prof. Pierre Brousset
. Prof. Jean-Pierre Delord
. Prof. Gilles Favre
. Dr. Nathalie Caunes-Hilary
. Prof. Sébastien Vergez
. Jean-Marc Perez

CRCT — **Scientific Director/Relations with the CRCT**: Prof. Gilles FAVRE

Medical Affairs Director: Prof. Jean-Pierre DELORD

Patient Care

Anesthesia	Dr. Sébastien PIERRE
Surgery	Prof. Sébastien VERGEZ
Hematology	Prof. Christian RECHER
Internal Medicine	Prof. Odile BEYNE-RAUZY
Oncogenetics	Prof. Rosine GUIMBAUD
Medical Oncology	Prof. Jean-Pierre DELORD
Radiotherapy	Prof. Elizabeth MOYAL
Brachytherapy	Prof. Isabelle BERRY
Intensive and Intermediate Care	Dr. Jean RUIZ
Supportive care	Dr. Nathalie CAUNES-HILARY

Medico-Technical Support and Research

Prof. Pierre BROUSSET	**Pathology Department**
Muriel POUBLANC	**Clinical Trials Office**
Dr. Fabien DESPAS	**Clinical Trials Office Hematology and Internal medicine**
Prof. Frédéric COURBON	**Imaging**
Prof. Gilles FAVRE	**Medical Biology Laboratory**
Prof. Eric DELABESSE	**Onco-Hematology Transfer Platform**
Dr. Jean-Marie CANONGE	**Hospital Pharmacy**
Régis FERRAND	**Medical Physics**
Bertrand DELPUECH	**Radiation Protection**
Prof. Anne GOMEZ-BROUCHET	**Cancer BioBank**

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

Medical Oncology
Prof. Jean-Pierre Delord

Supportive Care
Dr. Nathalie Caunes-Hilary

Oncogenetics
Prof. Rosine Guimbaud

Surgery
Prof. Sébastien Vergez
Operating rooms:
assistant head:
Dr. Alejandra Martinez

Hematology
Prof. Christian Récher

Internal Medicine
Prof. Odile Beyne-Rauzy

Brachytherapy
Prof. Isabelle Berry

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

Radiotherapy
Prof. Elizabeth Moyal
assistant head:
Dr. Michel Rives

Anesthesia
Dr. Sébastien Pierre

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
Prof. Anne Gomez-Brouchet

Medical Biology Laboratory
Prof. Gilles Favre

Hematology Laboratory
Prof. Eric Delabesse

Intensive Care
Dr. Jean Ruiz

Local networks

The IUCT-Oncopole is a member of several regional expert networks and contributes to the development of high-quality, innovative treatments for all patients in the Occitanie-Pyrénées area.

GENEPY

GENEPY is a cancer care network for women in the Midi-Pyrénées area who have a genetic predisposition to breast, ovarian, colorectal or endometrial cancer. Set up with support from the INCa and run by the Oncogenetics OCC, GENEPY facilitates and coordinates genetic screening, in line with INCa guidelines, in order to ensure every patient receives the best possible care.

ONCODIETS

2019 saw the regional launch of ONCODIETS, France's first network of independent cancer nutrition specialists, at a training day held at the IUCT-Oncopole in December. The ONCODIETS network enables independent nutritionists to work with cancer treatment centers in order to ensure continuity of care for patients when they leave hospital.

Onco-Occitanie

Onco-Occitanie is the name of the new regional cancer network formed when the OncoLR and Oncomip networks merged following the creation of the Occitanie Region in 2015. Its main missions are to coordinate cancer treatment across the region, to distribute reference documents and follow-up protocols, and to support the actions of the region's healthcare professionals. In 2019, Onco-Occitanie launched several projects that were of direct interest to the IUCT-Oncopole, including "3C & Réseau", which produced a 2019-2021 road map for the Occitanie region's 38 3C centers. The network accredited eleven IUCT multidisciplinary teams, including two inter-regional teams, which discussed 1,049 cases in 2019. It also facilitated the introduction of CART-T cell therapy for patients in the Occitanie-Pyrénées region (see p 57), created a regional geriatric oncology MOOC (p 55) and continued developing the AJAMIP (see p. 73) and oncofertility projects in the region. The network held its first Onco-Occitanie convention in Montpellier in September 2019.
http://www.onco-occitanie.fr/

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, which 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/

IUCT public interest group

The IUCT's collaborative dimension officially came into being via the creation of a public interest group (Groupement d'Intérêt Public – GIP) under a ministerial decree (Ministry for Social Affairs, Health and Women's Rights) issued on September 29, 2014, and published in the French Official Journal on October 10, 2014.
Currently presided by Prof. André Syrota, the IUCT GIP unites all the area's cancer treatment, research and training establishments, including the Institut Claudius Regaud, 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, as well as Toulouse Metropolitan Council, the Oncomip network (now Onco-Occitanie), the Ligue Contre le Cancer and the Fondation Toulouse Cancer Santé. Its Scientific Advisory Board's is composed of 13 practitioners and researchers from around the world:

- **Maria Blasco**
  Centro Nacional de Investigaciones Oncológicas, Madrid, Spain
- **Patrick Couvreur**
  Université Paris-Saclay, Paris, France
- **Anne Dejean**
  Institut Pasteur, Paris, France
- **Jean-Marc Egly**
  Institut de Génétique et de Biologie Moléculaire et Cellulaire, Strasbourg, France
- **Bruno Goud**
  Institut Curie, Paris, France
- **John Hickman**
  Coordinator IMI, Paris, France

Liselotte Hoejgaard
University of Copenhagen, Denmark
Cyril Kay
University of Alberta, Edmonton, Canada
Gillies McKenna - Cancer Research UK, Oxford, United Kingdom
Jacques Pouysségur
Institut de Recherche sur le Cancer et le Vieillissement, Nice, France
Josep Tabernero
Vall d'Hebron Institute of Oncology, Barcelona, Spain
William Vainchenker
Gustave Roussy, Villejuif, France
Benoit Van den Eynde
Ludwig Institute, Brussels, Belgium

One of the Scientific Advisory Board's most important tasks is to evaluate projects designed by the IUCT-Oncopole and CRCT and that request funding from the IUCT GIP and/or Fondation Toulouse Cancer Santé.
www.iuct.fr

Occitanie, a region where fewer people die of cancer

According to Santé Publique France's cancer map for 2019, male cancer death rates were lower in the Ariège, Aveyron, Haute-Garonne, Gers, Lot, Tarn and Tarn-et-Garonne départements than they were in the rest of France. Santé Publique France attributed this to earlier diagnosis of all types of tumor and more effective cancer care in Occitanie...

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 Claude 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, which it does via annual competitive grant schemes to fund innovative, interdisciplinary and collaborative projects sponsored by members of the Toulouse area's medical-scientific community. 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.
The FTCS and the IUCT GIP have the same scientific council.
https://www.toulousecancer.fr/

French Blood Service (Etablissement Français du Sang - EFS)

The French Blood Service has several facilities on the Oncopole site, including:
• A unit for sampling hematopoietic stem cells (HSC) from adults. This unit is based at the IUCT-Oncopole but provides sampling services for all three IUCTs (208 autologous HSC samples, 32 allogenic HSC samples and 3 lymphocyte/cell samples taken in 2019). In addition, since November 2019, it has performed erythrocytapheresis, mostly on patients with sickle cell disease (approximately 70 procedures per year).
• A cellular therapy unit (at the IUCT-Oncopole) to prepare and store bone marrow and stem cell samples. As well as catering to the three IUCTs, the unit responds to requests from other centers in the region, France and abroad (transfers in 2019: 134 autologous HSC samples, 61 allogenic HSC samples, 15 bone marrow samples and 28 mononucleated cells/2,850 grafts stored in liquid nitrogen).
• Both units are working closely with clinicians and pharmaceutical companies to roll out CAR-T cell therapy. In 2019, 10 patients were sampled and 8 patients were treated.
The French Blood Service also manages the Institute of Regenerative Medicine (INCERE), which houses the STROMALab mixed research unit (investigates the role and functions of adult stem cells, especially mesenchymal bone marrow cells and adipose tissues, and their use in regenerative medicine) and a start-up called Cell-Easy (develops innovative clinical production methods and technologies to accelerate the adoption of adult stem cells in regenerative medicine).
https://www.efs.sante.fr

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 round structured "return home" consultations, conducted in conjunction with the patient's family doctor. These consultations are coordinated by specially trained general practitioners who devote half their time to the system, working within cancer care centers, while continuing to spend the other half of their time in general practice. Five cancer centers across the Toulouse healthcare catchment area, including the IUCT-Oncopole, are currently testing the system, which has been baptized CREDO. Making it easier for caregivers to share information will 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.
A trial to test CREDO, supervised by Prof. M-E. Rougé-Bugat, has been funded by a DGOS (PREPS) grant. It will include 825 patients and will be completed at the end of 2020.

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 research groups. Most notably, Prof. J-P. Delord is vice-president of the Immuno-oncology Group (GIO), created in December 2016, and a member of the Scientific and Strategic Council.

In addition, the IUCT-Oncopole is a national expertise center for 16 INCa networks.
It is a regional referral center for 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)
- **REFCOR:** 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
(contact: Dr I. Rouquette)
- **RRePS:** Soft tissue and visceral sarcomas
(contact: Dr S. Le Guellec)
- **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)

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.

Catalonia-Occitanie Oncology Group (GOCO)

The Catalonia-Occitanie Oncology Group (GOCO) is an association of radiotherapy doctors, physicians, technicians and nurses in Catalonia and Occitanie that was set up in 1993 to promote disciplines relating to oncology, initial and continuing training, and exchanges between professionals working in oncology and associated disciplines. Its aims are to draw up standardized diagnosis and treatment protocols, and to develop basic and clinical research in oncology in southern Europe.

Organisation of European Cancer Institutes (OECI)

The IUCT-Oncopole has been a member of the Organisation of European Cancer Institutes (OECI) since 2018. In line with its founding objective of bringing together the critical mass of expertise and skills needed to further the development of personalized therapies, the OECI now has 82 member organizations, 11 of which are in France, which work together to ensure patients throughout Europe have access to the best possible treatment. Seven OECI experts carried out an audit of the IUCT-Oncopole in December 2019 to assess its application for accreditation as a Comprehensive Cancer Center. They should make their findings known in the summer of 2020.

European Network for Cutaneous Adverse Events to Oncologic Drugs (ENCADO)

ENCADO, the first European group focusing on dermatological toxicities and anticancer treatments, was founded by Dr V. Sibaud, in conjunction with Prof. G. Fabbrocini (Federico II University Hospital, Naples) and Dr A. Freites-Martinez (Fuaenlabrad University Hospital, Madrid). ENCADO's first official meeting took place in Madrid in October 2019, during the European Academy of Dermatology and Venerology's (EADV) annual congress. The network already has more than 30 members from 10 European countries. Results from its first two research projects will be published soon:

- Characterization of psoriasis induced by anticancer immunotherapy;
- Description of vitiligo induced by anti-CDK 4/6 treatments (ribociclib, palbociclib).

Another IUCT-Oncopole physician, Dr E. Vigarios, coordinates ENCADO's oral toxicity section. The network will hold its next meeting in Vienna in 2020.

European Neuroendocrine Tumor Society (ENETS)

In 2019, the IUCT-Oncopole and the IUCT-Rangueil Larrey became a European Neuroendocrine Tumor Society (ENETS) "European center of excellence for treating neuroendocrine tumor disease". The newly certified entity has been named "Toulouse University Center of Excellence for Neuroendocrine Tumors". This certification, awarded following an application process led by Prof. R. Guimbaud and Dr L. Dierickx, recognizes the center's multidisciplinary expertise in recruitment, diagnosis, treatment, clinical research and training doctors in a rare pathology - digestive neuroendocrine tumors. Only four centers in France have been awarded this certification (Paris, Lyon, Marseille and, now, Toulouse).

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. Its aim is to promote innovative, multi-center studies aimed at accelerating the development of anticancer drugs, especially for conditions for which there is as yet no therapeutic standard.

European Society of Gynaecological Oncology

The IUCT-Oncopole has been a European Society of Gynaecological Oncology (ESGO) accredited training center since 2017. The first diploma was awarded in 2019 to Dr C. Martinez Gomez. Only seven other centers in France are accredited to provide this high-level training.

II

BASIC AND TRANSLATIONAL RESEARCH

Cancer Research Center of Toulouse – CRCT

Key figures

21 basic and translational research **teams**

163 **researchers**

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

Presentation of the CRCT

The CRCT operates under the auspices of the National Institute for Health and Medical Research (Inserm) and the University of Toulouse III–Paul Sabatier. Its 21 research teams, 5 of which have CNRS accreditation, form the basic and translational research component of the IUCT-Oncopole healthcare center.

Missions

The CRCT is Toulouse's only dedicated cancer research center. Its teams' missions are to:

- Carry out basic research to determine the biological mechanisms underlying the appearance, progression and spread of cancers, and resistance to current treatments.
- Identify new ways of overcoming these mechanisms and discover new anti-cancer agents.
- Transfer findings from this basic research to clinical applications by designing translational research projects to test innovative approaches to diagnosis and treatment. The resulting medical applications benefit the IUCT-Oncopole's patients, while clinical data from the IUCT-Oncopole allows the CRCT's research teams to evaluate hypotheses.
- Integrate students and post-doctoral researchers into research teams so they can learn from more experienced researchers. This research-based training is complemented by a program of seminars and other scientific events to promote dialogue and interactions between disciplines.

Research themes

The CRCT focuses on four basic research themes:

- Oncogenic signaling, DNA damage and genetic instability
- RNA and cancer
- Tumor microenvironment and metabolism
- Oncoimmunology

And two transversal themes:

- Resistance mechanisms and new targets: from molecular pharmacology to clinical pharmacology
- Application of mathematical, physical and bioinformatics approaches to oncology.

CRCT teams are evaluated every 5 years

In 2019, the CRCT submitted its five-yearly renewal application to France's High Council for Evaluating Research and Higher Education (Hcéres), which then appointed a committee of experts from France and abroad to evaluate the CRCT's work. This committee visited the CRCT in November to conduct its audit.

Highlights

LabEx TOUCAN's successful renewal application and the funding granted to the "Cancer, Aging and Rejuvenation" (CARE) program were two major highlights of 2019. LabEx TOUCAN has now been renewed for five years with €3.5 million in funding, whereas the CARE project, which developed out of TOUCAN, was awarded a €5 million "University Research School" (EUR) grant.

Toulouse Cancer Laboratory of Excellence (LabEx TOUCAN) was set up to improve understanding of resistance mechanisms in blood cancers by focusing on two themes: the involvement of tumor cells and the role played by the tumor microenvironment. This research, led by Prof. Pierre Brousset, has generated more than 250 scientific papers and several patents. At the same time, LabEx TOUCAN has helped train young researchers, supported the CRCT's newer teams, and organized national and international conferences. In addition the LabEx label has facilitated collaborations with private laboratories, including ROCHE and Pierre Fabre, which support TOUCAN's projects on the tumor microenvironment, antitumor immunity, and the processing of microscopy imaging data, and with the LabEx CIMI (International Mathematics and Computing Center).
Indeed, analyzing big data has become a fundamental aspect of integrated approaches to studying cancer biology. It also forms a methodological link between TOUCAN's two objectives, as genome and transcriptome analyses and the processing of microscopy images generate large datasets. The renewal of the LabEx label will enable TOUCAN to strengthen its two core sections' ability to study tumor resistance at the single-cell level. The first section, which is part of the CRCT's technology cluster, focuses on single-cell RNA sequencing. It will use the TOUCAN-2 funding to extend its bioinformatics capability to collect and format data for storage in a data lake, and then to extract and analyze these data. The second section, housed in the IUCT-Oncopole's Pathology Laboratory, supervises the processing of digitized microscopy images and already has several cutting-edge tissue-analysis instruments and software packages. It will use the TOUCAN-2 funding to increase image acquisition and processing rates, and to improve and automate image segmentation and object recognition (especially after multiplex staining) by applying computational approaches such as deep learning.

Dr Vera Pancaldi's arrival at the CRCT, thanks to funding from Laboratoires Pierre Fabre and the Fondation Toulouse Cancer Santé, will further increase the consortium's computing power and will help the two facilities collect data and collate them in a single data lake. Integrative approaches to processing big datasets will provide an inexhaustible source of information on cancer resistance phenomena that will be used to identify biomarkers and therapeutic targets, and to further scientific knowledge.

Finally, TOUCAN-2 is also the basis of the "Cancer, Aging and Rejuvenation" University Research School (EUR CARE), which will provide grants for seven doctoral students within the consortium's teams and provide them with cutting-edge, transdisciplinary training.

EUR CARE is an international, research-led, transdisciplinary teaching program in the field of cancer, aging and bioengineering that is taught entirely in English and run in close collaboration with Toulouse's research centers. Coordinated by Prof. Philippe Valet (Institute of Cardiovascular and Metabolic Diseases – I2MC) and Prof. Bruno Ségui (CRCT), it will draw upon the cutting-edge research carried out by LabEx TOUCAN, the Gérontopole (a WHO Collaborating Center for research and training in aging) and the IUCT, as well as a network of international academic and industrial partners, and will stimulate scientific innovation, from basic principles to medical and industrial applications.

EUR CARE will draw on scientific concepts shared by the fields of aging and cancer and cover everything from basic mechanisms to new therapeutic strategies. Modules on the biomedical sciences are combined with innovative interdisciplinary courses that bring together physics, computing and mathematics. Students, most of whom will be recruited outside France, will be drawn from a variety of backgrounds, ranging from engineering to the hard sciences, exact sciences, and pharmaceutical and medical sciences. As of the first year of the master's program, they will be permanently based in an academic or industrial research laboratory in order to facilitate their research-led training.

Based at "Langlade Campus Biosanté", EUR CARE will increase the area's international attractiveness by promoting ambitious research linked to innovative development and training actions. The program's aims are to radically change the "classic" vertical training model by fostering creativity, promoting international collaborations between the worlds of academic and commercial research, and improving communication skills. This will encourage students to be proactive in their studies and career perspectives and prepare them to take up the professions being created by today's unprecedented advances in medicine and the biomedical sciences.

Research programs

Including numerous clinicians within the CRCT's teams helps ensure findings arising from basic research are rapidly transferred to clinical applications and that clinical data is made available for research. These integrated research programs are typified by the projects awarded funding through the Oncopole grant scheme.

In order to further research into immuno-oncology, in 2018 the Fondation Toulouse Cancer Santé, Inserm and the Pierre Fabre Research Institute set up the Chair of BioInformatics in Oncology. The position was awarded to Dr Vera Pancaldi, a physicist and expert in the biology of systems, who now leads CRCT team 21.

This initiative is part of an overall strategy to strengthen public-private partnerships in cancerology. For example, in December 2019 the CRCT, Pierre Fabre Research Institute and the IUCT-Larrey signed a multi-year framework agreement to develop alternative personalized therapies. "Alliance Oncopole", as this framework agreement is known, is a collegially governed program focusing on four themes:

- Converting patients' clinical and molecular data into molecular maps of tumors that can be used to determine the most suitable treatments. The Chair of BioInformatics in Oncology (CRCT team 21) will be in charge of analyzing data from patients at the IUCT-Oncopole.
- Drawing on the expertise of the IUCT-Oncopole's and CRCT's clinicians and researchers to provide support to certain Pierre Fabre Research Institute projects.
- Combining the CRCT's research expertise with Pierre Fabre's industrial know-how in order to rapidly transform newly discovered therapeutic targets into drug candidates.
- Organizing annual scientific workshops where international experts and Alliance Oncopole teams can discuss the latest advances in cancer research.

Moreover, two annual grant schemes provide funding for local, innovative and collaborative projects. The first, known as @IUCT-Oncopole, supports projects run by IUCT-Oncopole clinicians and CRCT researchers; the second, administered by the Fondation Toulouse Cancer Santé, supports interdisciplinary projects conducted by researchers from Toulouse's scientific community.

@IUCT-Oncopole grants for translational research projects

Every year, the IUCT-Oncopole uses research-oriented donations to fund selected translational research projects, which have received additional funding from the Fondation Toulouse Cancer Santé since 2018.
@IUCT-Oncopole's objective is to encourage innovative, transdisciplinary projects involving at least one IUCT-Oncopole clinical team and one CRCT research team. Proposals are evaluated by an external scientific board. The most recent @IUCT-Oncopole call for projects, at the end of 2019, attracted five applications, which will be evaluated and selected during 2020.

Joint IUCT GIP — Fondation Toulouse Cancer Santé annual grant scheme

The Fondation Toulouse Cancer Santé, a major partner of the IUCT Public Interest Group, supports numerous initiatives, including innovative, interdisciplinary and collaborative research projects by the Toulouse's medical-scientific community. The aim is to encourage research teams to present the sort of high-risk research projects that are often the source of tomorrow's scientific, technological and economic breakthroughs.
The Fondation Toulouse Cancer Santé, in conjunction with the IUCT Public Interest Group's Research College, chose "Metabolism & Cancer" as the theme for its 9th grant scheme. As a prelude to the call for projects, a workshop on this theme was held on February 4, 2019, with numerous posters and oral presentations, including by researchers from outside the IUCT, most notably Kevin M. Brindle (University of Cambridge), Eyal Gottlieb (Technion Institute, Haifa), Laurent Le Cam (IRCM, Montpellier), and Mariia Yuneva (Francis Crick Institute, London).

After assessing all the applications, the International Scientific Board and the Fondation Toulouse Cancer Santé granted funding to the following three projects involving the CRCT.

Melanoma, sphingolipid metabolism and response to TNF: from basic mechanisms to immunotherapy in patients with advanced melanoma

Coordinator: Prof. Bruno Ségui - CRCT team 4

Partners: Prof. Nicolas Meyer - IUCT-Oncopole, CRCT; Thomas Filleron - IUCT-Oncopole

Although immune checkpoint inhibitors (ICIs) have revolutionized the treatment of metastatic melanoma, many patients do not respond to these therapies. Recent work by the team has shown that TNF has an important role in inhibiting CD8+ T-cell dependent anti-tumor responses and in the resistance of melanoma to PD-1 inhibitors. These discoveries formed the basis for two clinical trials, conducted at the IUCT-Oncopole, for patients with advanced melanoma:
- TICIMEL, a phase-Ib trial to evaluate tolerance to combining ICI with TNF inhibitors,
- MELANF, a pilot study to identify resistance signatures to TNF-dependent ICIs.

Preliminary results show that TNF modifies sphingolipid (SL) metabolism in melanoma cells. SL metabolism may contribute to TNF-dependent ICI resistance mechanisms.
The current project aims to determine: (i) the role of SL metabolism in TNF-dependent ICI resistance in melanoma mouse models and (ii) the impact of TNF inhibitors on SL metabolism in melanoma patients being treated with ICIs. Results could lead to the development of new immunotherapies and to the stratification of melanoma patients for ICI treatment.

Systemic redistribution of metabolic flows during chemotherapy in acute myeloid leukemia - HIJACKAML

Coordinator: Prof. Jean-Charles Portais - Stromalab

Partner: Dr Jean-Emmanuel Sarry - CRCT team 18

Despite a high rate of complete remission after intensive chemotherapy, the overall prognosis for patients with acute myeloid leukemia (AML) is poor and the relapse rate is high, especially due to the presence of chemo-resistant leukemic clones. Earlier results obtained by the consortium show that CLRs have a high oxidative and mitochondrial metabolism with high oxidation of fatty acids. In addition, leukemic blasts are able to reprogram the glucose metabolism to their benefit and induce hyperinsulinemia, thereby indicating a remote metabolic control of organs by the tumor. However, the impact of chemotherapy on systemic metabolism is currently unknown. The HIJACKAML consortium will examine i) how the redistribution of metabolic flows favors the survival of leukemia cells, ii) the impact of chemotherapy on systemic metabolism and iii) the way in which the redistribution of metabolic flows after chemotherapy favors the survival of resistant leukemia cells.
This project will extend understanding of the mechanisms underlying the development chemo-resistant leukemia clones and identify and validate the functioning of new metabolic targets for treating AML.

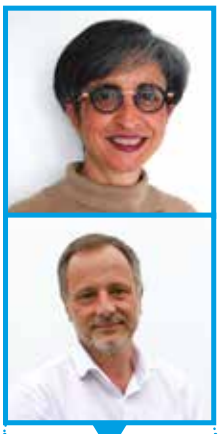
Development of innovative inhibitors targeting cholesterol metabolism deregulations in breast cancer: towards new therapeutic strategies - OCDOKill

Coordinator: Dr Marc Poirot - CRCT team 12

Partner: Prof. Florence Dalenc - IUCT-Oncopole, CRCT team 12

Breast cancer is the main cause of cancer deaths in women, so there is an urgent need to find new therapeutic strategies. The team has shown that the enzyme that converts cortisol into cortisone produces a tumor-promoting metabolite, OCDO, in both estrogen receptor-positive and estrogen receptor-negative breast cancers. Concentrations of this enzyme and of OCDO are higher in breast cancer tissues than in normal tissues and are correlated with a higher risk of death. Consequently, the enzyme may be a new therapeutic target that could lead to the development of new anti-cancer treatments.
The project's objectives are i) to identify enzyme inhibitors that specifically target the production of OCDO and ii) to more precisely determine the link between OCDO production, enzyme expression and the infiltration of regulatory T cells (Treg) in breast cancers. Results could lead to the development of new immunotherapies.

The CRCT has 21 teams whose research is supported by an onsite, state-of-the-art Technology Cluster with its own staff.



01
M. Ayyoub / J.P Delord

02
MJ Pillaire

03
G. Favre

04
T. Levade /
N. Andrieu

05
S. Millevoi

06
S. Pyronnet /
C. Bousquet

07
P. Brousset / F. Meggetto

08
S. Manenti

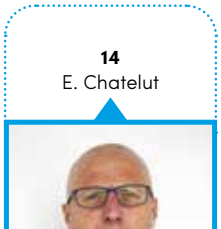
09
J.J. Fournié

10
P. Cordelier

11
E. Moyal /
C. Toulas

12
M. Poirot / S. Silvente-Poirot

13
H. Avet-Loiseau /
L. Martinet



14
E. Chatelut

15
M. Bardiès

16
E. Delabesse

17
J. Guillermet-Guibert

18
J.E. Sarry

19
F. Chibon

20
S. Valitutti

21
V. Pancaldi

Pôle technologique
F. Lopez

TEAM 1 Antitumor immunity and immunotherapy

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

Keywords: T cell antitumor response, tumor antigens, lymphocyte exhaustion, immune checkpoint modulators, anti-cancer 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 to decipher 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 for responses to immunotherapy and to the development of combination therapies, in particular 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 2019

1. 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, Feliu 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**. Accepted
2. Montfort A, Dufau C, Colacios C, Andrieu-Abadie N, Levade T, Filleron T, Delord JP, Ayyoub M, Meyer N, Ségui B. Anti-TNF, a magic bullet in cancer immunotherapy? **J Immunother Cancer.** 2019 Nov 14;7(1):303. doi: 10.1186/s40425-019-0802-y
3. Franchini DM, Lanvin O, Tosolini M, Patras de Campaigno E, Cammas A, Péricart S, Scarlata CM, Lebras M, Rossi C, Ligat L, Pont F, Arimondo PB, Laurent C, Ayyoub M, Despas F, Lapeyre-Mestre M, Millevoi S*, Fournié*. Microtubule-driven stress granule dynamics regulates inhibitory immune checkpoints expression in T cells. **Cell Rep**. 2019 Jan 2;26(1):94-107.e7.

TEAM 2 Regulation of DNA replication and genetic instability in cancers

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leader: Dr Marie-Jeanne Pillaire

Keywords: Replicative stress, genetic instability and replication
Funding sources: ANR 2016-2019, "2R-POL" Program (Coord.: J-S. Hoffmann), INCa PLBIO 2016-2019 (Coord.: J-S. Hoffmann), Ligue Nationale contre le Cancer (Label), Ligue Régionale (Coord.: J-S. Hoffmann/R. Guimbaud), Inserm/Occitanie Regional Council (Coord.: M-J. Pillaire)
Research theme: The team focuses on the mechanisms that limit genetic instability, whether via responses to replication stress or via DNA repair processes, as these mechanisms are altered in many cancer cells. Results obtained by the team as part of a collaborative study led to the identification of a mechanism by which cells with a defective response to replicative stress show replication defects and therefore proliferation defects (1). The team has shown that, in some cancers, overexpression of proteins associated with replication forks can protect against replication stress (2). Studies also show that deregulation of MCM8/9 repair proteins facilitates the development of myeloid tumors (3).

Major publications in 2019

1. González Besteiro MA, Calzetta NL, Loureiro SM, Habif M, Bétous R, Pillaire MJ, Maffia A, Sabbioneda S, Hoffmann JS, Gottifredi V. Chk1 loss creates replication barriers that compromise cell survival independently of excess origin firing. **EMBO J.** 2019 Jul 11:e101284. doi: 10.15252/embj.2018101284. PMID:31294866
2. Bianco JN, Bergoglio V, Lin YL, Pillaire MJ, Schmitz AL, Gilhodes J, Lusque A, Mazières J, Lacroix-Triki M, Roumeliotis TI, Choudhary J, Moreaux J, Hoffmann JS, Tourrière H, Pasero P. Overexpression of Claspin and Timeless protects cancer cells from replication stress in a checkpoint-independent manner. **Nat Commun**. 2019 Feb 22;10(1):910. doi: 10.1038/s41467-019-08886-8. PMID:30796221
3. Lutzmann M, Bernex F, da Costa de Jesus C, Hodroj D, Marty C, Plo I, Vainchenker W, Tosolini M, Forichon L, Bret C, Queille S, Marchive C, Hoffmann JS, Méchali M. MC M8- and MCM9 Deficiencies Cause Lifelong Increased Hematopoietic DNA Damage Driving p53-Dependent Myeloid Tumors. **Cell Rep**. 2019 Sep 10;28(11):2851-2865.e4. doi: 10.1016/j.celrep.2019.07.095. PMID:31509747

TEAM 3 Cancer cell signaling and therapeutics

TEAM ACCREDITED BY THE FONDATION POUR LA RECHERCHE MÉDICALE

Team leader: Prof. Gilles Favre

Keywords: RTK/RAS/ERK, Rho GTPases, DNA double-strand breaks, resistance to targeted therapies, nanobodies, split GFP, liquid biopsy, clinical trials, lung cancers, melanoma

Funding sources: Fondation pour la Recherche Médicale, Fondation ARC, Fondation de France, Ligue Contre le Cancer, ANR, AstraZeneca, Inserm Transfert, Cis-Bio, Occitanie Regional Council

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 2019

1. De Magis A, Manzo SG, Russo M, Marinello J, Morigi R, Sordet O, Capranico G. DNA damage and genome instability by G-quadruplex ligands are mediated by R loops in human cancer cells. **Proc Natl Acad Sci USA**. 2019 Jan 15;116(3):816-825. doi: 10.1073/pnas.1810409116. PMID:30591567
2. Calvayrac O, Nowosad A, Cabantous S, Lin LP, Figarol S, Jeannot P, Serres M, Callot C, Perchey RT, Creff J, Taranchon-Clermont E, Rouquette I, Favre G, Pradines A, Manenti S, Mazieres J, Lee H, Besson A. Cytoplasmic p27Kip1 promotes tumorigenesis via suppression of RhoB activity. **J Pathol.** 2019 Jan;247(1):60-71. 2019 Jan;247(1):60-71. doi: 10.1002/path.5167. PMID:30206932
3. Bery N, Keller L, Soulié M, Gence R, Iscache AL, Cherier J, Cabantous S, Sordet O, Lajoie-Mazenc I, Pedelacq JD, Favre G, Olichon A. A Targeted Protein Degradation Cell-Based Screening for Nanobodies Selective toward the Cellular RHOB GTP-Bound Conformation. **Cell Chem Biol.** 2019 Nov 21;26(11):1544-1558.e6. doi: 10.1016/j.chembiol.2019.08.009. PMID:31522999
4. 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.** 2019 Oct 31. pii: 126896. doi: 10.1172/JCI126896. PMID:31671073
5. Cristini A, Ricci G, Britton S, Salimbeni S, Huang SN, Marinello J, Calsou P, Pommier Y, Favre G, Capranico G, Gromak N, Sordet O. Dual Processing of R-Loops and Topoisomerase I Induces Transcription-Dependent DNA Double-Strand Breaks. **Cell Rep.** 2019 Sep 17;28(12):3167-3181.e6. doi: 10.1016/j.celrep.2019.08.041. PMID:31533039

TEAM 4 Sphingolipid metabolism, cell death and tumor progression

PROGRAM ACCREDITED BY THE FONDATION ARC 2019

Team leaders: Prof. Thierry Levade and Dr Nathalie Andrieu-Abadie

Keywords: Ceramide, sphingosine 1-phosphate, melanoma, oncometabolism, oncoimmunology, tumor microenvironment, tumor necrosis factor, TNF

Funding sources: Ligue Contre le Cancer, ERA-NET Transcan-2, Inserm Transfert, Cancéropôle GSO, BMS, ANR, IUCT-O, Société Française de Dermatologie, Fondation ARC

Research theme: The team studies how sphingolipid metabolism is involved in tumor progression, focusing on the interactions between melanoma cells and their microenvironment and on modulating the antitumor immune response.

Most recently, the team's research has shown that:

- TNF or TNFR1 blockade synergizes with anti-PD-1 antibodies in antitumor immune responses in preclinical models of melanomas.
- Weak expression of the acid ceramidase ASAH1 is associated with invasive phenotype in melanomas via the integrin alpha-V beta5/FAK signaling pathway.
- Several alterations in ceramide metabolism contribute to melanomas' resistance to BRAF inhibitors.
- Sphingosine kinase inhibition greatly increases the efficacy of immunotherapy in preclinical cancer models.

Major publications and patents in 2019

1. Garandeau D, Noujarede J, Leclerc J, Imbert C, Garcia V, Bats ML, Rambow F, Gilhodes J, Filleron T, Meyer N, Brayer S, Arcucci S, Tartare-Deckert S, Segui B, Marine JC, Levade T, Bertolotto C*, Andrieu-Abadie N* (co-last). Targeting the Sphingosine 1-Phosphate Axis Exerts Potent Antitumor Activity in BRAFi-Resistant Melanomas. **Mol Cancer Ther**. 2019 Feb; 18(2): 289-300. doi: 10.1158/1535-7163.MCT-17-1141. PMID:30482853

2. Montfort A, Dufau C, Colacios C, Andrieu-Abadie N, Levade T, Filleron T, Delord JP, Ayyoub M, Meyer N, Ségui B. Anti-TNF, a magic bullet in cancer immunotherapy? **J Immunother Cancer**. 2019 Nov 14;7(1):303. doi: 10.1186/s40425-019-0802-y. PMID:31727152

3. Leclerc, J., Garandeau, D., Pandiani, C., Gaudel, C., Bille, K., Nottet, N., Garcia, V., Colosetti, P., Pagnotta, S., Bahadoran, P., Tondeur, G., Mograbi, B., Dalle, S., Caramel, J., Levade, T., Ballotti, R., Andrieu-Abadie, N*. and Bertolotto, C* (co-last). Lysosomal acid ceramidase ASAH1 controls the transition between invasive and proliferative phenotype in melanoma cells. **Oncogene**. 2019 Feb;38(8): 1282-1295. doi: 10.1038/s41388-018-0500-0. PMID:30254208

4. Colacios C, Andrieu-Abadie N, Levade T, Ségui B, Meyer N, Lamant L, Imbert C. Use of sk1 as biomarker for predicting response to immune checkpoint inhibitors. WO2019162325, 2019.

5. Ghenassia A, Ségui B, Levade T, Andrieu-Abadie N. Use of SK2 inhibitors in combination with immune checkpoint blockade therapy for the treatment of cancer. EP19305461.6, 2019

TEAM 5 RNA-binding proteins and post-transcriptional regulation in cancer

Team leaders: Dr Stefania Millevoi

Keywords: Post-transcriptional gene expression, RNA binding proteins, translation, RNA regulons, RNA G-quadruplex structures, glioblastoma

Funding sources: Fondation de France, Ligue Contre le Cancer

Research theme: The team's aim is to clarify the role of RNA binding proteins in cancer cells and thereby determine how genome expression is reprogrammed and how RNA-protein networks are modulated by oncogenic signaling and DNA damage. This basic research has high translational potential in the fields of:

- Immunotherapy (work carried out in collaboration with CRCT team 9, led by Jean-Jacques Fournié)
- Resistance to radiochemotherapy for glioblastoma (work carried out in collaboration with CRCT team 11, led by Elizabeth Moyal and Christine Toulas) and for head and neck cancers (projects led by Anouchka Modesto, who is both a member of CRCT team 5 and a radiation oncologist at the IUCT-Oncopole).

Major publications in 2019

1. Franchini DM, Lanvin O, Tosolini M, Patras de Campaigno E, Cammas A, Péricart S, Scarlata CM, Lebras M, Rossi C, Ligat L, Pont F, Arimondo PB, Laurent C, Ayyoub M, Despas F, Lapeyre-Mestre M, Millevoi S*, Fournié*. Microtubule-driven stress granule dynamics regulates inhibitory immune checkpoints expression in T cells. **Cell Rep**. 2019 Jan 2;26(1):94-107.e7. doi: 10.1016/j.celrep.2018.12.014. PMID:30605689

2. Mubaid S, Ma JF, Omer A, Ashour K, Lian XJ, Sanchez BJ, Robinson S, Cammas A, Dormoy-Raclet V, Di Marco S, Chittur SV, Tenenbaum SA, Gallouzi IE. HuR counteracts miR-330 to promote STAT3 translation during inflammation-induced muscle wasting. **Proc Natl Acad Sci U S A**. 2019 Aug 27;116(35):17261-17270. doi: 10.1073/pnas.1905172116. PMID:31405989

3. Modesto A, Chira C, Sol JC, Lubrano V, Boulinguez S, Pagès C, Sibaud V, Gomez-Roca C, Moyal É, Meyer N. Treatment of patients with brain metastases from a melanoma. **Cancer Radiother.** 2019 Apr;23(2):147-150. doi: 10.1016/j.canrad.2018.05.006. Review. French. PMID:30904418

4. Modesto A, Galissier T, Lusque A, Delord JP, Uro-Coste E, Sarini J, Mouchet F, Lopez R, Laprie A, Graff P, Vergez S, Rives M. Definitive radiochemotherapy or initial surgery for oropharyngeal cancer : To what extent can p16 expression be used in the decision process? **Strahlenther Onkol**. 2019 Jun;195(6):496-503. doi: 10.1007/s00066-019-01451-8. PMID:30877351

5. Cargnello M, Topisirovic I. c-Myc steers translation in lymphoma. **J Exp Med**. 2019Jul 1;216(7):1471-1473. doi: 10.1084/jem.20190721. PMID:31209069

TEAM 6 Protein synthesis and secretion in oncogenesis

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leaders: Dr Stéphane Pyronnet and Dr Corinne Bousquet

Keywords: Protein synthesis, mRNA translation, signaling pathways, tumor microenvironment, somatostatin, pancreatic cancer, acute myeloid leukemia
Funding sources: Ligue Contre le Cancer, LabEx TOUCAN, ANR, INCa PLBIO, PAIR Pancréas, Fondation BMS, Fondation Toulouse Cancer Santé, Fondation de France
Research theme: The team investigates the roles of protein synthesis and secretion in pancreatic cancers and acute myeloid leukemia (AML), and whether these processes can be targeted for therapeutic intervention. Current research projects on these two types of malignancy focus on the translational regulation of gene expression and carcinogenesis, the targeting of protein synthesis in pancreatic cancers, and the tumor microenvironment. This work has revealed the importance of tumor microenvironment heterogeneity and the value of using the anti-secretory action of somatostatin analogues to target its pro-tumor activity.

Major publications in 2019

1. Neuzillet C, Tijeras-Raballand A, Ragulan C, Cros J, Patil Y, Martinet M, Erkan M, Kleeff J, Wilson J, Apte M, Tosolini M, Wilson AS, Delvecchio FR, Bousquet C, Paradis V, Hammel P, Sadanandam A, Kocher HM. Inter- and intra-tumoural heterogeneity in cancer-associated fibroblasts of human pancreatic ductal adenocarcinoma. **J Pathol**. 2019 May;248(1):51-65. doi: 10.1002/path.5224. PMID:30575030

2. Alard A, Marboeuf C, Fabre B, Jean C, Martineau Y, Lopez F, Vende P, Poncet D, Schneider RJ, Bousquet C, Pyronnet S. Differential Regulation of the Three Eukaryotic mRNA Translation Initiation Factor (eIF) 4Gs by the Proteasome. **Front Genet**. 2019 Mar 29;10:254. doi: 10.3389/fgene.2019.00254. eCollection 2019. PMID:30984242

3. Goehrig D, Nigri J, Samain R, Wu Z, Cappello P, Gabiane G, Zhang X, Zhao Y, Kim IS, Chanal M, Curto R, Hervieu V, de La Fouchardière C, Novelli F, Milani P, Tomasini R, Bousquet C, Bertolino P, Hennino A. Stromal protein βig-h3 reprogrammes tumour microenvironment in pancreatic cancer. **Gut**. 2019 Apr;68(4):693-707. doi: 10.1136/gutjnl-2018-317570. PMID:30415234

4. Jaud M, Philippe C, Van Den Berghe L, Ségura C, Mazzolini L, Pyronnet S, Laurell H, Touriol C. The PERK Branch of the Unfolded Protein Response Promotes DLL4 Expression by Activating an Alternative Translation Mechanism. **Cancers** (Basel). 2019 Jan 25;11(2). pii: E142. doi: 10.3390/cancers11020142. PMID:30691003

5. Müller D, Shin S, Goullet de Rugy T, Samain R, Baer R, Strehaiano M, Masvidal-Sanz L, Guillermet-Guibert J, Jean C, Tsukumo Y, Sonenberg N, Marion F, Guilbaud N, Hoffmann JS, Larsson O, Bousquet C, Pyronnet S, Martineau Y. eIF4A inhibition circumvents uncontrolled DNA replication mediated by 4E-BP1 loss in pancreatic cancer. **JCI Insight.** 2019 Nov 1;4(21). pii: 121951. doi: 10.1172/jci.insight.121951. PMID:31672935

6. Saponaro C, Gmyr V, Thévenet J, Moerman E, Delalleau N, Pasquetti G, Coddeville A, Quenon A, Daoudi M, Hubert T, Vantyghem MC, Bousquet C, Martineau Y, Kerr-Conte J, Staels B, Pattou F, Bonner C. The GLP1R Agonist Liraglutide Reduces Hyperglucagonemia Induced by the SGLT2 Inhibitor Dapagliflozin via Somatostatin Release. **Cell Rep**. 2019 Aug 6;28(6):1447-1454.e4. doi: 10.1016/j.celrep.2019.07.009. PMID:31390560

TEAM 7 RNA biology in hematological cancers

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leaders: Prof. Pierre Brousset and Dr Fabienne Meggetto

Keywords: miRNA, lncRNA, acute myeloid leukemia, anaplastic large cell lymphoma, ALK, targeted therapy, ER stress, resistance
Funding sources: ANR, Ligue Contre le Cancer, LabEx TOUCAN, Fondation ARC, Fondation pour la Recherche Médicale, Association Laurette Fugain, Institut CALYM, Fondation Fonroga
Research theme: The team's research focuses on the role of non-coding RNA (ncRNA) in regulating cell pathways involved in the development and progression of cancer. To this end, it is exploring the expression profiles and functions of microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), their interactions with proteins and their protein-coding potential in chemoresistant hematological malignancies. Its goals are to assess the physiological and pathological roles of these ncRNAs, ascertain the impact of their deregulation on prognosis, tumor progression and responses to treatment, and identify the upstream mechanisms of ncRNA regulation.

Major publications in 2019

1. Hoareau-Aveilla C, Quelen C, Congras A, Caillet N, Labourdette D, Dozier C, Brousset P, Lamant L, Meggetto F. MiR-497 suppresses cycle progression through an axis involving CDK6 in ALK-positive cells. **Haematologica**. 2019 Feb;104(2):347-359. doi: 10.3324/haematol.2018.195131. PMID:30262555

2. Torossian A, Broin N, Frentzel J, Daugrois C, Gandarillas S, Al Saati T, Lamant L, Brousset P, Giuriato S, Espinos E. Blockade of crizotinib-induced BCL2 elevation in ALK-positive anaplastic large cell lymphoma triggers autophagy associated with cell death. **Haematologica**. 2019 Jul;104(7):1428-1439. doi: 10.3324/haematol.2017.181966. PMID:30679328

3. Jaud M, Philippe C, Van Den Berghe L, Ségura C, Mazzolini L, Pyronnet S, Laurell H, Touriol C. The PERK Branch of the Unfolded Protein Response Promotes DLL4 Expression by Activating an Alternative Translation Mechanism. **Cancers** (Basel). 2019 Jan 25;11(2). pii: E142. doi: 10.3390/cancers11020142. PMID:30691003

4. Gourvest M, Brousset P, Bousquet M. Long Noncoding RNAs in Acute Myeloid Leukemia: Functional Characterization and Clinical Relevance. **Cancers** (Basel). 2019 Oct 24;11(11). pii: E1638. doi: 10.3390/cancers11111638. Review. PMID:31653018

5. Fuchs S, Naderi J, Meggetto F. Non-Coding RNA Networks in ALK-Positive Anaplastic-Large Cell Lymphoma. **Int J Mol Sci**. 2019 Apr 30;20(9). pii: E2150. doi: 10.3390/ijms20092150. PMID:31052302

TEAM 8 Cell cycle and autophagy in myeloid malignancies

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leader: Dr Stéphane Manenti

Keywords: Cell cycle, autophagy, signaling, acute myeloid leukemia (AML), checkpoints, tyrosine kinases
Funding sources: Ligue Contre le Cancer (2016-2020), Cancéropole GSO
Research theme: The team studies the mechanisms by which signaling pathways activated by oncogenes (mutated tyrosine kinases) create new modifications in these proteins (phosphorylation, transcriptional or post-transcriptional regulation, miRNA) and thereby regulate key proteins in the cell cycle (CDC25A, CHK1). It is also investigating new functions of CHK1 and CDC25A.
Another research program focuses on how autophagy regulates signaling pathways (signalophagy) in AML. The team is investigating the impact of these proteins in the cell cycle and the role of autophagy in AML cancer cells' responses and resistance to therapeutic agents, with the aim of identifying new therapeutic targets. Results have highlighted the roles of the transcription factor ATF4 in inducing autophagy, of CHK1 and Pim2 in mitosis, of CHK1 as a prognostic factor and therapeutic target, and of ubiquitin-specific protease-7 (USP7) as a CHK1 regulator and therapeutic target in AML.

Major publications and patents in 2019

1. Larrue C, Heydt Q, Saland E, Boutzen H, Joffre C, Sarry JE, Récher C. Oncogenic KIT mutations induce STAT3-dependent autophagy to support cell proliferation in acute myeloid leukemia. **Oncogenesis**. 2019 Jul 16;8(8):39. doi: 10.1038/s41389-019-0148-9. PMID:31311917

2. Calvayrac O, Nowosad A, Lin LP, Figarol S, Jeannot P, Serres MP, Callot C, Perchey RT, Creff J, Taranchon-Clermont E, Favre G, Pradines A, Manenti S, Mazieres J, Lee H, and Besson A. Cytoplasmic p27/Kip1 promotes tumorigenesis via the suppression of RhoB activity. **J Pathol**. 2019 Jan;247(1):60-71. doi: 10.1002/path.5167. PMID:30206932

3. Largeaud L, Bérard E, Bertoli S, Dufrechou S, Prade N, Gadaud N, Tavitian S, Bories P, Luquet I, Sarry A, De Mas V, Huguet F, Delabesse E, Récher C. Outcome of AML patients with IDH2 mutations in real world before the era of IDH2 inhibitors. **Leuk Res**. 2019 Apr 27;81:82-87. doi: 10.1016/j.leukres.2019.04.010. PMID:31055247

4. Comont T, Delavigne K, Cougoul P, Bertoli S, Delabesse E, Fenaux P, Beyne-Rauzy O. Management of myelodysplastic syndromes in 2019: An update. **Rev Med Interne**. 2019 Sep;40(9):581-589. doi: 10.1016/j.revmed.2019.04.001. PMID:31054780

5. Bertoli S, Paubelle E, Bérard E, Saland E, Thomas X, Tavitian S, Larcher MV, Vergez F, Delabesse E, Sarry A, Huguet F, Larrue C, Bosc C, Farge T, Sarry JE, Michallet M, Récher C. Ferritin heavy/light chain (FTH1/FTL) expression, serum ferritin levels, and their functional as well as prognostic roles in acute myeloid leukemia. **Eur J Haematol**. 2019 Feb;102(2):131-142. doi: 10.1111/ejh.13183. PMID:30325535

6. Brevet : Use of USP7 inhibitors for the treatment of acute myeloid leukemia BIO18527 – MANENTI / MC. Dépôt N° EP19305181.0

TEAM 9 Therapeutic innovations in B lymphomas

Team leader: Dr Jean-Jacques Fournié

Keywords: Lymphoma, MALC models, data mining, bioinformatics, deep learning, single-cell RNAseq, therapy, drugs, immune checkpoints, flow cytometry
Funding sources: LabEx Toulouse Cancer, Ligue Contre le Cancer, Fondation ARC, Fondation Toulouse Cancer Santé, POCTEFA, imCore Roche
Research theme: The team's research involves using scRNA-seq to identify innate immunity cells and detect them in tumors so they can be used in immunotherapy treatments for lymphomas. In 2019, the team conducted the world's first study of human Tγδ lymphocytes (1) and designed a bioinformatics tool for detecting them. This research also discovered a new immune-checkpoint control mechanism in these lymphocytes that can be used to simultaneously regulate the synthesis of all these inhibitor receptors (3). This process offers great potential for developing new anticancer drugs (4-6).

Major publications in 2019

1. Pizzolato G, Kaminski H, Tosolini M, Franchini DM, Pont F, Martins F, Valle C, Labourdette D, Cadot S, Quillet-Mary A, Poupot M, Laurent C, Ysebaert L, Meraviglia S, Dieli F, Merville P, Milpied P, Déchanet-Merville J, Fournié JJ. Single-cell RNA sequencing unveils the shared and the distinct cytotoxic hallmarks of human TCRVδ1 and TCRVδ2 γδ T lymphocytes. **Proc Natl Acad Sci U S A**. 2019 Jun 11;116(24):11906-11915. doi: 10.1073/pnas.1818488116. PMID:31118283

2. Pont F, Tosolini M, Fournié JJ. Single-Cell Signature Explorer for comprehensive visualization of single cell signatures across scRNA-seq datasets. **Nucleic Acids Res**. 2019 Jul 11. pii: gkz601. doi: 10.1093/nar/gkz601. PMID:31294801

3. Franchini DM, Lanvin O, Tosolini M, Patras de Campaigno E, Cammas A, Péricart S, Scarlata CM, Lebras M, Rossi C, Ligat L, Pont F, Arimondo PB, Laurent C, Ayyoub M, Despas F, Lapeyre-Mestre M, Millevoi S, Fournié JJ. Microtubule-Driven Stress Granule Dynamics Regulate Inhibitory Immune Checkpoint Expression in T Cells. **Cell Rep**. 2019 Jan 2;26(1):94-107.e7. doi: 10.1016/j.celrep.2018.12.014. PMID:30605689.

4. Franchini DM, Lanvin O, Curdy N, Fournié JJ. Control of lymphocyte activity by stress granules. New targets for immunotherapy ? **Med Sci** (Paris). 2019 Jun-Jul;35(6-7):507-509. doi: 10.1051/medsci/2019109. PMID:31274077

5. Curdy N, Lanvin O, Laurent C, Fournié JJ, Franchini DM. Regulatory Mechanisms of Inhibitory Immune Checkpoint Receptors Expression. **Trends Cell Biol**. 2019 Oct;29(10):777-790. doi: 10.1016/j.tcb.2019.07.002. Review.

6. Rossi C, Gravelle P, Decaup E, Bordenave J, Poupot M, Tosolini M, Franchini DM, Laurent C, Morin R, Lagarde JM, Ysebaert L, Ligat L, Jean C, Savina A, Klein C, Cespedes AM, Perez-Galan P, Fournié JJ, Bezombes C. "Boosting Gammadelta T Cell-Mediated Antibody-Dependent Cellular Cytotoxicity by Pd-1 Blockade in Follicular Lymphoma." **Oncoimmunology**. 2019; 8(3): 1554175. doi: 10.1080/2162402X.2018.1554175. eCollection 2019. PMID:30723586

TEAM 10 Molecular heterogeneity of pancreatic tumors

Team leader: Dr Pierre Cordelier

Keywords: Pancreatic cancer, oncogenesis mechanisms, innovative therapies, biomarkers
Funding sources: Ligue Contre le Cancer, imCore Genentech, Fondation Toulouse Cancer Santé, Fondation de France, RHU, Occitanie Regional Council, Inserm.
Research theme: Even though pancreatic adenocarcinoma is relatively rare, late diagnosis and the ineffectiveness of current treatments mean that this form of cancer is forecast to be the second largest cause of cancer deaths worldwide by 2030. The team's goal is to determine the molecular bases underlying the formation of pancreatic tumor resistance to current therapies, most notably innovative biotherapies and especially oncolytic therapies, and thereby develop innovative treatments, particularly gene therapies, to improve care for these patients. In 2019, the team's clinicians helped demonstrate that venous thromboembolism is a frequent event in patients with pancreatic cancer and is associated with poor outcomes (1). From a basic research perspective, the team, in collaboration with researchers in Barcelona, has continued investigating the role of microRNAs in the formation of pancreatic tumors (2). Finally, the team has written overviews in the field of liquid biopsies and their technological challenges (3,4), and a review of the literature on cytidine deaminase, an interesting new target for cancer therapies (5).

Major publications in 2019

1. Frere C, Bournet B, Gourgou S, Fraisse J, Canivet C, Connors JM, Buscail L, Farge D, BACAP Consortium. Incidence of Venous Thromboembolism in Patients with Newly Diagnosed Pancreatic Cancer and Factors Associated With Outcomes. **Gastroenterology**. 2019 Dec 13. doi: 10.1053/j.gastro.2019.12.009. PMID:31843588
2. Diaz-Riascos ZV, Ginesta MM, Fabregat J, Serrano T, Busquets J, Buscail L, Cordelier P, Capellá G. Expression and Role of MicroRNAs from the miR-200 Family in the Tumor Formation and Metastatic Propensity of Pancreatic Cancer. **Mol Ther Nucleic Acids**. 2019 Jun 29;17:491-503. doi: 10.1016/j.omtn.2019.06.015. PMID:31336236
3. Buscail E, Maulat C, Muscari F, Chiche L, Cordelier P, Dabernat S, Alix-Panabières C, Buscail L. Liquid Biopsy Approach for Pancreatic Ductal Adenocarcinoma. **Cancers** (Basel). 2019 Jun 19;11(6). pii: E852. doi: 10.3390/cancers11060852. Review. PMID:31248203
4. Cacheux J, Bancaud A, Leichlé T, Cordelier P. Technological Challenges and Future Issues for the Detection of Circulating MicroRNAs in Patients With Cancer. **Front Chem**. 2019 Nov 28, 7, 815. eCollection 2019. Review. PMID:31850308
5. Frances A, Cordelier P. The Emerging Role of Cytidine Deaminase in Human Diseases: A New Opportunity for Therapy? **Mol Ther**. 2019 Dec 6. pii: S1525-0016(19)30552-0. doi: 10.1016/j.ymthe.2019.11.026. Review. PMID:31870623

TEAM 11 Glioblastoma (GBM) resistance to radiotherapy: from signaling pathways to clinical trials

Team leaders: Prof. Elizabeth Moyal and Dr Christine Toulas

Keywords: Glioblastoma, radioresistance, heterogeneity, reprogramming, migration, stem cells, transdifferentiation, FGFR, integrins, metabolic imaging, biomarkers, radioimmunotherapy
Funding sources: Aviesan, INCa, Inserm, Fondation ARC, Ligue Contre le Cancer, ARTC, PHUC CAPTOR, Incyte, AstraZeneca, Bayer
Research theme: The team's objective is to optimize radiotherapy for patients with glioblastoma. To this end, it is exploring three research themes: intrinsic radioresistance, including the role of integrins and growth-factor signaling pathways, especially FGFRs; 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 partly confirmed, in partnership with drug companies, by their inhibition by pharmacological inhibitors are tested in the clinic. Furthermore, in order to optimize the effectiveness of radiation therapy against a variety of tumors, especially glioblastoma, brain metastases, head and neck cancers and esophageal cancers, the IUCT-Oncopole's Radiotherapy Department is conducting clinical trials of several radioimmunotherapy treatments. These trials are combined with ancillary biological and imaging studies to identify response profiles to these combinations, which are carried out by the team in conjunction with both CRCT team 1 and other French research teams specializing in imaging.
Hence, the team coordinates and conducts several national and international research projects. MoGlimaging, a project involving eight teams across France, was set up with funding from ITMO Cancer to model and determine the heterogeneity of therapeutic resistance mechanisms in glioblastoma. SI2GMA, funded by the ARC's SIGN'IT program, brings together five teams to deter-

mine a multiparameter biological and imaging profile of therapeutic responses to a combined stereotactic radiotherapy and Durvalumab treatment for patients with relapsed glioblastoma and included in the IUCT-Oncopole's phase II STERIMGLI trial, coordinated by E Moyal. Finally, an international collaboration funded by Worldwide Cancer UK with Dr Valiente (Spanish National Cancer Research Center) is studying the correlation between a tumor marker and the microenvironment of brain metastases of lung cancer, and their clinical radiation sensitivity. This study, conducted in collaboration with the Pathology and Radiotherapy Departments, is the subject of a medical doctoral thesis being prepared by one of the department's interns.

Major publications in 2019

1. Malric L, Monferran S, Delmas C, Arnauduc F, Dahan P, Boyrie S, Deshors P, Lubrano V, Da Mota DF, Gilhodes J, Filleron T, Siegfried A, Evrard SM, Kowalski-Chauvel A, Cohen-Jonathan Moyal E*, Toulas C*, Lemarié A*. Inhibiting Integrin β8 to Differentiate and Radiosensitize Glioblastoma-initiating Cells. **Mol Cancer Res**. 2019 Feb;17(2):384-397. doi: 10.1158/1541-7786.MCR-18-0386. PMID:30266751.*Co-last authors

2. Deshors P, Toulas C, Arnauduc F, Malric L, Siegfried A, Nicaise Y, Lemarié A, Larrieu D, Tosolini M, Cohen-Jonathan Moyal E, Courtade-Saidi M, Evrard SM. Ionizing radiation induces endothelial transdifferentiation of glioblastoma stem-like cells through the Tie2 signaling pathway. **Cell Death Dis.** 2019 Oct 28;10(11):816. doi: 10.1038/s41419-019-2055-6. PMID:31659157

3. Kowalski-Chauvel A, Gouaze-Andersson V, Baricault L, Martin E, Delmas C, Toulas C, Cohen-Jonathan-Moyal E, Seva C. Alpha6-Integrin Regulates FGFR1 Expression through the ZEB1/YAP1 Transcription Complex in Glioblastoma Stem Cells Resulting in Enhanced Proliferation and Stemness. **Cancers** (Basel). 2019 Mar 22;11(3). pii: E406. doi: 10.3390/cancers11030406. PMID:30909436

4. Appay R, Dehais C, Maurage CA, Alentorn A, Carpentier C, Colin C, Ducray F, Escande F, Idbaih A, Kamoun A, Marie Y, Mokhtari K, Tabouret E, Trabelsi N, Uro-Coste E, Delattre JY, Figarella-Branger D; POLA Network (E Cohen-Moyal belongs to authors). CDKN2A homozygous deletion is a strong adverse prognosis factor in diffuse malignant IDH-mutant gliomas. **NeuroOncol**. 2019; 21(12):1519-1528

5. Laprie A, Ken S, Filleron T, Lubrano V, Vieillevigne L, Tensaouti F, Catalaa I, Boetto S, Khalifa J, Attal J, Peyraga G, Gomez-Roca C, Uro-Coste E, Noel G, Truc G, Sunyach MP, Magné N, Charissoux M, Supiot S, Bernier V, Mounier M, Poublanc M, Fabre A, Delord JP, Cohen-Jonathan Moyal E. Dose-painting multicenter phase III trial in newly diagnosed glioblastoma: the SPECTRO-GLIO trial comparing arm A standard radiochemotherapy to arm B radiochemotherapy with simultaneous integrated boost guided by MR spectroscopic imaging. **BMC Cancer**. 2019 Feb 21;19(1):167. doi: 10.1186/s12885-019-5317-x. PMID:30791889

TEAM 12 Cholesterol metabolism and therapeutic innovations

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

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

Keywords: Cholesterol, metabolism, oxysterols, dendrogenin, OCDO, tumor suppressor/promoter, breast cancer, cell differentiation and death, autophagy, immunity, exosome, tamoxifen, SERM, enzymes, nuclear receptors, medicinal chemistry
Funding sources: Institut National du Cancer (PRTK, PLBIO), Fondation Toulouse Cancer Santé, Ligue Nationale 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 which disappears during carcinogenesis in favor of the second molecule, 6-oxo-cholestan-diol (OCDO), which is a tumor promoter. The team is currently characterizing this new metabolic branch of the cholesterol pathway in mammary glands and in different sub-types of breast cancer. It is also studying the properties of these molecules in order to explore possible new therapies and to obtain a better understanding of the mechanisms underlying both acquired and intrinsic resistance to conventional treatments.

Major publications in 2019

1. Bauriaud-Mallet M, Vija-Racaru L, Brillouet S, Mallinger A, de Medina P, Rives A, Payre B, Poirot M, Courbon F, Silvente-Poirot S. The cholesterol-derived metabolite dendrogenin A functionally reprograms breast adenocarcinoma and undifferentiated thyroid cancer cells. **J Steroid Biochem Mol Biol**. 2019 Jun 3;192:105390. doi: 10.1016/j.jsbmb.2019.105390. PMID:31170473

2. Poirot M, Silvente-Poirot S. Cholesterol metabolism and therapeutic innovations. Oxysterols: an expanding family of structurally diversified bioactive steroids. **J Steroid Biochem Mol Biol**. 2019 Jul 31:105443. doi: 10.1016/j.jsbmb.2019.105443. PMID:31376459

3. Soulès R, Audouard-Combe F, Huc-Claustre E, de Medina P, Rives A, Chatelut E, Dalenc F, Franchet C, Silvente-Poirot S, Poirot M, Allal B. A fast UPLC-HILIC method for an accurate quantification of dendrogenin A in human tissues. **J Steroid Biochem Mol Biol**. 2019 Aug 12;194:105447. doi: 10.1016/j.jsbmb.2019.105447. PMID:31415823

4. Bertucci F, Ng CKY, Patsouris A, Droin N, Piscuoglio S, Carbuccia N, Soria JC, Dien AT, Adnani Y, Kamal M, Garnier S, Meurice G, Jimenez M, Dogan S, Verret B, Chaffanet M, Bachelot T, Campone M, Lefeuvre C, Bonnefoi H, Dalenc F, Jacquet A, De Filippo MR, Babbar N, Birnbaum D, Filleron T, Le Tourneau C, André F. Genomic characterization of metastatic breast cancers. **Nature**. 2019 May;569(7757):560-564. doi: 10.1038/s41586-019-1056-z. Epub 2019 May 22. Erratum in: Nature. 2019 Aug;572(7767):E7. PMID:31118521

5. D'Hondt V, Canon JL, Roca L, Levy C, Pierga JY, Le Du F, Campone M, Desmoulins I, Goncalves A, Debled M, Rios M, Ferrero JM, Serin D, Hardy-Bessard AC, Piot G, Brain E, Dohollou N, Orfeuvre H, Lemonnier J, Roché H, Delaloge S, Dalenc F. UCBG 2-04: Long-term results of the PACS 04 trial evaluating adjuvant epirubicin plus docetaxel in node-positive breast cancer and trastuzumab in the human epidermal growth factor receptor 2-positive subgroup. **Eur J Cancer**. 2019 Nov;122:91-100. doi: 10.1016/j.ejca.2019.09.014. Epub 2019 Oct 18. PMID:31634648

TEAM 13 Oncogenomics and immunology of multiple myeloma

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, Fondation pour la Recherche Médicale, Ligue Contre le Cancer, Cancéropôle GSO

Research theme: The team's objectives are mostly translational and aimed at improving the therapeutic management of patients with multiple myeloma (MM) in order to prolong survival. Access to the world's largest tumor bank enables the team to pursue three main research themes:

- Use of large-scale genome sequencing of tumors to guide clinicians' therapeutic choices by identifying patients who are likely to respond to different treatments.
- Characterization of MM patients' immune systems so they can be activated to eliminate tumor cells.
- Analysis of interactions between tumor cells and normal bone marrow cells, in particular mesenchymal stem cells.

Major publications in 2019

1. Thakurta A, Ortiz M, Blecua P, Towfic F, Corre J, Serbina NV, Flynt E, Yu Z, Yang Z, Palumbo A, Dimopoulos MA, Gutierrez NC, Goldschmidt H, Sonneveld P, Avet-Loiseau H. High subclonal fraction of 17p deletion is associated with poor prognosis in multiple myeloma. **Blood**. 2019 Mar 14;133(11):1217-1221. doi: 10.1182/blood-2018-10-880831. PMID:30692124

2. Perrot A, Lauwers-Cances V, Tournay E, Hulin C, Chretien ML, Royer B, Dib M, Decaux O, Jaccard A, Belhadj K, Brechignac S, Fontan J, Voillat L, Demarquette H, Collet P, Rodon P, Sohn C, Lifermann F, Orsini-Piocelle F, Richez V, Mohty M, Macro M, Minvielle S, Moreau P, Leleu X, Facon T, Attal M, Avet-Loiseau H, Corre J. Development and validation of a cytogenetic prognostic index predicting survival in multiple myeloma. **J Clin Oncol**. 2019 Jul 1;37(19):1657-1665. doi: 10.1200/JCO.18.00776. PMID:31091136

3. Moreau P, Attal M, Hulin C, Arnulf B, Belhadj K, Benboubker L, Bene MC, Broijl A, Caillon H, Caillot D, Corre J, Delforge M, Dejoie T, Doyen C, Facon T, Sonntag C, Fontan J, Garderet L, Jie KS, Karlin L, Kuhnowski F, Lambert J, Leleu X, Lenain P, Macro M, Mathiot C, Orsini-Piocelle F, Perrot A, Stoppa AM, Ven de Donk N, Wuilleme S, Zweegman S, Kolb B, Touzeau C, Roussel M, Tiab M, Marolleau JP, Meulement N, Vekemans MC, Westerman M, Klein SK, Levin MD, Fermand JP, Escoffre-Barbe M, Eveillard JR, Garidi R, Ahmadi T, Zhuang S, Chiu C, Pei L, de Boer C, Smith E, Deraedt W, Kampfenkel T, Schecter J, Vermeulen J, Avet-Loiseau H, Sonneveld P. Daratumumab plus bortezomib, thalidomide, and dexamethasone versus bortezomib, thalidomide, and dexamethasone alone before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): final analysis results of part 1 of a randomised, open-label, phase 3 study. **The Lancet**. 2019 Jul 6;394(10192):29-38. doi: 10.1016/S0140-6736(19)31240-1. Epub 2019 Jun 3. Erratum in: Lancet. 2019 Jun 14. PMID:31171419

4. Guillerey C, Nakamura K, Pichler AC, Barkauskas D, Krumeich S, Stannard K, Miles K, Harjunpää H, Yu Y, Casey M, Doban AI, Lazar M, Hartel G, Smith D, Vuckovic S, Teng MW, Bergsagel PL, Chesi M, Hill GR, Martinet L, Smyth MJ. Chemotherapy followed by anti-CD137 mAb immunotherapy improves disease control in a mouse myeloma model. **JCI Insight.** 2019 Jun 13;5. pii: 125932. doi: 10.1172/jci.insight.125932. PMID:31194697

Munshi NC, Jagannath S, Avet-Loiseau H. Monoclonal Gammopathy May Be of Unpredictable Significance. **JAMA Oncol.** 2019 Jul 18. doi: 10.1001/jamaoncol.2019.1580. PMID:3131838

TEAM 14 Dose individualization of anticancer drugs

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 interindividual 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 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 2019

1. Le Louedec F, Alix-Panabières C, Lafont T, Allal BC, Garrel R, Digue L, Guigay J, Cupissol D, Delord JP, Lallemant B, Alfonsi M, Aubry K, Mazel M, Becher F, Perriard F, Chatelut E, Thomas F. Cetuximab Pharmacokinetic/Pharmacodynamics relationships in advanced head and neck carcinoma patients. **Br J Clin Pharmacol**. 2019 Jun;85(6):1357-1366. doi: 10.1111/bcp.13907. PMID:30811063

2. Paludetto MN, Puisset F, Chatelut E, Arellano C. Identifying the reactive metabolites of tyrosine kinase inhibitors in a comprehensive approach: Implications for drug-drug interactions and hepatotoxicity. **Med Res Rev**. 2019 Nov;39(6):2105-2152. doi: 10.1002/med.21577. doi: 10.1002/med.21577. Review. PMID:31111528

3. Paludetto MN, Stigliani JL, Robert A, Bernardes-Génisson V, Chatelut E, Puisset F, Arellano C. Involvement of Pazopanib and Sunitinib Aldehyde Reactive Metabolites in Toxicity and Drug-Drug Interactions *in Vitro* and in Patient Samples. **Chem Res Toxicol**. Epub 2019 Sep 26. doi: 10.1021/acs.chemrestox.9b00205. PMID:31535851

4. 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, Suc E, Sillet Bach I, Filleron T, Roché H, Chatelut E, White-Koning M, Thomas F. Factors affecting tamoxifen metabolism in breast cancer patients; preliminary results of the French PHACS study (NCT01127295). **Clin Pharmacol Ther.** 2019 Sep;106(3):585-595. doi: 10.1002/cpt.1404. PMID: 30786012

5. Puszkiel A, Bauriaud-Mallet M, Bourgeois R, Dierickx L, Courbon F, Chatelut E. Evaluation of the Interaction of Amino Acid Infusion on ^{177}Lu-Dotatate Pharmacokinetics in Patients with Gastroenteropancreatic Neuroendocrine Tumors. **Clin Pharmacokinet**. 2019 Feb;58(2):213-222. doi: 10.1007/s40262-018-0674-1. PMID:29736841

TEAM 15 Multiscale dosimetry for radiotherapy optimization

Team leader: Dr Manuel Bardiès

Keywords: Dosimetry, Monte-Carlo modeling, therapy optimization
Funding sources: AIEA, Medirad (Euratom), MRT Dosimetry (EuraMET), ANR
Research theme: The team uses measurements and models of radiation transport at different scales, from cell to patient, to optimize internal and external radiotherapy. It is currently working on two major projects:
- Dositest (http://dositest.fr/index.html) is a multi-center study that uses Monte-Carlo modeling of scintigraphic imaging and dosimetry to compare clinical dosimetry approaches in molecular radiotherapy. The sub-programs comprising this long-term project are financed by a variety of sources (IAEA, Euratom, EuraMET);
- OpenDose (https://opendose.org) aims to generate dosimetric reference data for molecular radiotherapy (17 partners).

Major publications in 2019

1. Chiesa C, Bardiès M, Zaidi H.Voxel-based dosimetry is superior to mean absorbed dose approach for establishing dose-effect relationship in targeted radionuclide therapy. **Med Phys**. 2019 Oct 4. doi: 10.1002/mp.13851. PMID:31584697
2. Delbaere A, Younes T, Vieillevigne L. On the conversion from dose-to-medium to dose-to-water in heterogeneous phantoms with Acuros XB and Monte Carlo calculations. **Phys Med Biol**. 2019 Oct 4;64(19):195016. doi: 10.1088/1361-6560/ab3df3. PMID:31437832
3. Ladjohounlou R, Lozza C, Pichard A, Constanzo J, Karam J, Le Fur P, Deshayes E, Boudousq V, Paillas S, Busson M, Le Blay M, Jarlier M, Marcatili S, Bardiès M, Bruchertseifer F, Morgenstern A, Torgue J, Navarro-Teulon I, Pouget JP. Drugs That Modify Cholesterol Metabolism Alter the p38/JNK-Mediated Targeted and Nontargeted Response to Alpha and Auger Radioimmunotherapy. **Clin Cancer Res**. 2019 Aug 1;25(15):4775-4790. doi: 10.1158/1078-0432.CCR-18-3295. PMID:31061069
4. Pichard A, Marcatili S, Karam J, Constanzo, J, Ladjohounlou R, Courteau A, Jarlier M, Bonnefoy N, Patzke S, Stenberg V, Coopman P, Cartron G, Navarro-Teulon I, Repetto-Llamazares A, Heyerdahl H, Dahle J, Bardiès M, Pouget JP. The therapeutic effectiveness of (177)Lu-lilotomab in B-cell non-Hodgkin lymphoma involves modulation of G2/M cell cycle arrest. **Leukemia** 2019 Dec 13;10.1038/s41375-019-0677-4. doi:10.1038/s41375-019-0677-4. PMID:31836849
5. Sakata D, Kyriakou I, Tran HN, Bordage MC, Rosenfeld A, Ivanchenko V, Incerti S, Emfietzoglou D, Guatelli S. Electron track structure simulations in a gold nanoparticle using Geant4-DNA. **Phys Med**. 2019 Jul;63:98-104. doi: 10.1016/j.ejmp.2019.05.023. PMID:31221415

TEAM 16 Alteration of transcription factors in acute leukemias

Team leader: Prof. Eric Delabesse

Keywords: Acute leukemia, transcription factors, Pax5, Gata2
Funding sources: ANR, INCa, Ligue Contre le Cancer, Fondation ARC, Occitanie Regional Council, 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 stem cells develop into different types of blood cells. This process takes place mostly in bone marrow and is finely regulated both by extrinsic factors, brought in by bone marrow cells, and by intrinsic factors to the stem cell, such as transcription factors (TF). Stem cells differentiate into functional (mature) cells according to an individual's needs.
Deregulation of hematopoiesis at an early stage can lead to acute leukemia (AL), in which the blockage of stem cell differentiation leads to uncontrolled proliferation of immature cells, which flood the marrow and then the blood. The team's work, which lies at the interface between clinical and basic research, is aimed at improving AL diagnosis and developing alternative therapies. This involves identifying genomic alterations in transcription factors (TF) in AL patients and then modeling these alterations in cell culture models and mouse models in order to ascertain their role in the leukemia process. This knowledge can then be applied to developing new therapies.
The team is exploring mutations acquired during lifespan and inherited mutations associated with a predisposition to leukemia. These investigations recently enabled the team to identify recurrent mutations in AL patients that involve two TFs: PAX5 and GATA2. The team recreated these mutations in mouse models in order to study leukemia transformation and relapse mechanisms.

Major publications in 2019

1. Fournier B, Balducci E, Duployez N, Clappier E, Cuccuini W, Arfeuille C, Caye-Eude A, Delabesse E, Bottollier-Lemallaz Colomb E, Nebral K, Chrétien ML, Derrieux C, Cabannes-Hamy A, Dumezy F, Etancelin P, Fenneteau O, Frayfer J, Gourmel A, Loosveld M, Michel G, Nadal N, Penther D, Tigaud I, Fournier E, Reismüller B, Attarbaschi A, Lafage-Pochitaloff M, Baruchel A. B-ALL With t(5;14)(q31;q32); IGH-IL3 Rearrangement and Eosinophilia: A Comprehensive Analysis of a Peculiar IGH-Rearranged B-ALL. **Front Oncol**. 2019 Dec 10;9:1374. doi: 10.3389/fonc.2019.01374. eCollection 2019. PMID:31921638
2. Largeaud L, Bérard E, Bertoli S, Dufrechou S, Prade N, Gadaud N, Tavitian S, Bories P, Luquet I, Sarry A, De Mas V, Huguet F, Delabesse E, Récher C. Outcome of AML patients with IDH2 mutations in real world before the era of IDH2 inhibitors. **Leuk Res**. 2019 Apr 27;81:82-87. doi: 10.1016/j.leukres.2019.04.010. PMID:31055247
3. Largeaud L, Bertoli S, Bérard E, Dufrechou S, Prade N, Gadaud N, Tavitian S, Bories P, Luquet I, Sarry A, Mas V, Huguet F, Delabesse E, Récher C. Outcome of relapsed/refractory AML patients with IDH1R132 mutations in real life before the era of IDH1 inhibitors. **Leuk Lymphoma**. 2019 Sep 30:1-4. doi: 10.1080/10428194.2019.1668937. PMID:31566052
4. Lopez CK, Noguera E, Stavropoulou V, Robert E, Aid Z, Ballerini P, Bilhou-Nabera C, Lapillonne H, Boudia F, Thirant C, Fagnan A, Arcangeli ML, Kinston SJ, Diop M, Job B, Lecluse Y, Brunet E, Babin L, Villeval JL, Delabesse E, Peters AHFM, Vainchenker W, Gaudry M, Masetti R, Locatelli F, Malinge S, Nerlov C, Droin N, Lobry C, Godin I, Bernard OA, Gottgens B, Petit A, Pflumio F, Schwaller J, Mercher T. Ontogenic changes in hematopoietic hierarchy determine pediatric specificity and disease phenotype in fusion oncogene-driven myeloid leukemia. **Cancer Discov**. 2019 Oct 29. pii: CD-18-1463. doi: 10.1158/2159-8290.CD-18-1463. PMID:31662298
5. Passet M, Boissel N, Sigaux F, Saillard C, Bargetzi M, Ba I, Thomas X, Graux C, Chalandon Y, Leguay T, Lengliné E, Konopacki J, Quentin S, Delabesse E, Lafage-Pochitaloff M, Pastoret C, Grardel N, Asnafi V, Lhéritier V, Soulier J, Dombret H, Clappier E; Group for Research on Adult ALL (GRAALL). PAX5 P80R mutation identifies a novel subtype of B-cell precursor acute lymphoblastic leukemia with favorable outcome. **Blood**. 2019 Jan 17;133(3):280-284. doi: 10.1182/blood-2018-10-882142. PMID:30510083

TEAM 17 SIGDYN – PI3K isoforms, signaling and cancerogenesis

Team leader: Dr Julie Guillermet-Guibert

Keywords: KRAS signaling, signaling lipids, in vivo oncogenic signaling, genetically modified mouse models, pancreatic carcinogenesis, phosphoproteomics, adaptive resistance, targeted therapies, cell plasticity, advanced solid tumors

Funding sources: Horizon 2020 MSCA-ITN, Fondation de France, Fondation Toulouse Cancer Santé, Cancéropôle GSO, LabEx Toucan

Research theme: The signaling pathway controlled by PI3K plays a central role in cell proliferation, survival, differentiation, migration and metabolism. PI3K class 1 is a family of four enzymes with non-redundant functions. PI3K activation is a very common event in tumors and is associated with resistance to previous exposure to targeted therapies.

The team's objective is to identify early signals of resistance mechanisms associated with PI3K in order to offer patients effective new therapeutic combinations. Phase I and phase II trials have tested both pan-PI3K and isoform-specific PI3K inhibitors, but they are difficult to use. Specific inhibitors are more promising and should enable advanced solid tumors to be treated.

Major publications in 2019

1. Müller D, Shin S, Goullet de Rugy T, Samain R, Baer R, Strehaiano M, Masvidal-Sanz L, Guillermet-Guibert J, Jean C, Tsukumo Y, Sonenberg N, Marion F, Guilbaud N, Hoffmann JS, Larsson O, Bousquet C, Pyronnet S, Martineau Y. eIF4A inhibition circumvents uncontrolled DNA replication mediated by 4E-BP1 loss in pancreatic cancer. **JCI Insight.** 2019 Nov 1;4(21). pii: 121951. doi: 10.1172/jci.insight.121951. PMID:31672935

2. Therville N, Arcucci S, Vertut A, Ramos-Delgado F, Da Mota DF, Dufresne M, Basset C, Guillermet-Guibert J. Experimental pancreatic cancer develops in soft pancreas: novel leads for an individualized diagnosis by ultrafast elasticity imaging. Theranostics. 2019 Aug 14;9(22):6369-6379. doi: 10.7150/thno.34066. eCollection 2019. PMID:31588223

3. Zamora A, Alves M, Chollet C, Therville N, Fougeray T, Tatin F, Franchet C, Gomez-Brouchet A, Vaysse C, Martinez LO, Najib S, Guillermet-Guibert J, Lacazette E, Prats AC, Garmy-Susini B. Paclitaxel induces lymphatic endothelial cells autophagy to promote metastasis. **Cell Death Dis**. 2019 Dec 20;10(12):956. doi: 10.1038/s41419-019-2181-1. PMID:31863036

TEAM 18 RESIST@ML – Drug resistance and oncometabolism in acute myeloid leukemia (AML)

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

Team leader: Dr Jean-Emmanuel Sarry

Keywords: Leukemia, drug resistance, PDX, mitochondria, oncometabolism, catabolic flexibility, clonal heterogeneity, cancer stem cells, inflammation, signaling, innovative therapeutics, cytarabine (AraC), fatty acid (FA), bone marrow ecosystem

Funding sources: Ligue Nationale et Régionale de Lutte Contre le Cancer, PIA-PSPC IMODI, LabEx Toucan, PHUC CAPTOR, Fondation Toulouse Cancer Santé, GILEAD Hemato-Oncology Research Fellowship Grant, Fondation ARC, Fondation de France – Fonds pour la Lutte Contre le Cancer, H2020-MSCA-IF-GF-2019, Occitanie Regional Council, Programme Hubert Curien Germaine de Staël, Interreg POCTEFA

Research theme: The team's goal is to understand and target the metabolic mechanisms responsible for therapeutic resistance in AML. Metabolomic, transcriptomic, pharmacological and functional approaches are being combined with xenograft models and samples from patients in order to investigate the ways in which resistance mechanisms are impacted by (i) mitochondrial energy production and metabolic flexibility; (ii) interactions between leukemic blasts and stromal cells; and (iii) potential regulators of metabolic and energy pathways. This research has already shown that AraC-resistant AML cells have a "HIGH OxPHOS" gene signature, dependent on fatty acid oxidation, and overexpress the CD36 fatty acid transporter. This phenotype results from the induction of a transcriptional program in response to mitochondrial stress, which regulates mitochondrial homeostasis, redox and energy metabolism. Preliminary results strongly suggest that this mechanism is pleotropic and induced in response to other AML treatments. The team has produced a preclinical xenograft model that it is using to predict responses to AraC (and other targeted therapies) in mice and patients, characterize chemoresistance, identify new therapeutic targets and predict patient relapse. Results will help clinicians determine the most appropriate therapy for patients.

Major publications in 2019

1. Stuani L, Sabatier M, Wang F, Poupin N, Bosc C, Saland E, Castelli F, Gales L, Monter-

sino C, Boet E, Turtoi E, Kaoma T, Farge T, Broin N, Larrue C, Baran N, Conti M, Loric S, Mouchel PL, Gotanègre M, Cassan C, Fernando L, Cognet G, Zavoriti A, Hosseini M, Boutzen H, Morita K, Futreal A, Chu-Van E, Le Cam L, Carroll M, Selak M, Vey N, Calmettes C, Pigneux A, Bidet A, Castellano R, Fenaille F, Turtoi A, Cazals G, Bories P, Gibon Y, Nicolay B, Ronseaux S, Marszalek J, DiNardo C, Konopleva M, Collette Y, Linares L, Bellvert F, Jourdan F, Takahashi K, Récher C, Portais JC, Sarry JE. Combinatory therapy targeting mitochondrial oxidative phosphorylation improves efficacy of IDH mutant inhibitors in acute myeloid leukemia. **bioRxiv** 749580; doi: https://doi.org/10.1101/749580

2. Aroua N, Ghisi M, Boet E, 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, Syrykh C, Laurent C, Gotanègre M, Bonnefoy N, Bellvert F, Portais JC, Nicot N, Azuale F, Kaoma T, Tamburini J, Vergez F, Récher C, Sarry JE. Extracellular ATP and CD39 activate cAMP-mediated mitochondrial stress response to promote cytarabine resistance in acute myeloid leukemia. **bioRxiv** 806992; doi: https://doi.org/10.1101/806992

3. Hosseini M, Rezvani H, Aroua N, Bosc C, Farge F, Saland E, Guyonnet-Dupérat V, Zaghdoudi S, Jarrou L, Larrue C, Sabatier M, Mouchel PL, Gotanègre M, Piechaczyk M, Bossis G, Récher C,Sarry JE. Targeting Myeloperoxidase Disrupts Mitochondrial Redox Balance and Overcomes Cytarabine Resistance in Human Acute Myeloid Leukemia. **Cancer Res**. 2019 Oct 15;79(20):5191-5203. doi: 10.1158/0008-5472.CAN-19-0515. PMID:31358527

4. Stuani L, Sarry JE. Help from outside: cysteine to survive in AML. **Blood**. 2019 Jul 25;134(4):336-338. doi: 10.1182/blood.2019001580. PMID:31345926

5 . Stuani L, Sabatier M, Sarry JE. Exploiting Metabolic Dependencies and Flexibility for Personalized Therapy in Acute Myeloid Leukemia. **BMC Biol**. 2019 Jul 18;17(1):57. doi:

TEAM 19 ONCOSARC – Oncogenesis of sarcomas

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

Team leader: Dr Frédéric Chibon

Keywords: Sarcoma, genetics, genomics, chromosome, metastasis, oncogenesis

Funding sources: AVIESAN/ITMO Cancer, Fondation ARC, Fondation pour la Recherche Médicale, Liddy Shriver Sarcoma Initiative, patients' charities

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. In order to more fully understand these oncogenesis mechanisms, the team is now focusing on two aspects of pleomorphic sarcomas: i) genome alterations, via an exhaustive study conducted using whole genome and transcriptome sequencing approaches; and ii) cellular mechanisms, in particular, the tumor-cell fusion the team has observed in these tumors and first described in a paper in 2019.

Because the ultimate aim is to improve treatment for patients, the team is also developing tools to improve diagnosis and monitor the clinical evolution of patients. Having previously identified and validated an almost universal prognostic expression signature in sarcomas, the team is now working on turning this signature into a practical tool for patient care. Major grants awarded by the INCa in 2018 enabled the team to launch two clinical trials, including one at the IUCT-Oncopole, to assess the potential use of this signature. One of these trials is a translational study aimed at describing the immunological landscape of rare sarcomas (PRTK-2018); the other will test the impact on patient treatment of the transcriptomic signature developed by the team (PHRC-2018). The team continued this work in 2019, orienting its translational research towards single tumor cells, especially cells circulating in patients' blood.

Major publications in 2019

1. Valentin T, Lesluyes T, Le Guellec S, Chibon F. Chemotherapy in Localized Soft Tissue Sarcoma: Will We Soon Have to Treat Grade 1 Tumours? Update on CINSARC Performances. Ann. Oncol. 2019 Jan 1;30(1):153-155. doi: 10.1093/annonc/mdy465. PMID:30335133

2. Croce S, Lesluyes T, Delespaul L, Bonhomme B, Pérot G, Velasco V, Mayeur L, Rebier F, Ben Rejeb H, Guyon F, McCluggage WG, Floquet A, Querleu D, Chakiba C, Devouassoux-Shisheboran M, Mery E, Arnould L, Averous G, Soubeyran I, Le Guellec S, Chibon F. GREB1-CTNNB1 Fusion Transcript Detected by RNA-Sequencing in a Uterine Tumor Resembling Ovarian Sex Cord Tumor (UTROSCT): A Novel CTNNB1 Rearrangement. Genes Chromosomes Cancer. 2019 Mar;58(3):155-163. doi: 10.1002/gcc.22694. Epub 2019 Jan 7. PMID:30350331

3. Croce S, Lesluyes T, Valle C, M'Hamdi L, Thébault N, Pérot G, Stoeckle E, Noël JC, Fontanges Q, Devouassoux-Shisheboran M, Querleu D, Guyon F, Floquet A, CHakiba C, Mayeur L, Rebier F, MacGrogan G, Soubeyran I, Le Guellec S, Chibon F. The NanoCind® signature is an independent prognosticator of recurrence and death in uterine leiomyosarcomas. Clin Cancer Res. 2019 Dec 3. pii: clincanres.2891.2019. doi: 10.1158/1078-0432.CCR-19-2891. PMID:31796515

4. Delespaul L, Merle C, Lesluyes T, Lagarde P, Le Guellec S, Pérot G, Baud J, Carlotti M, Danet C, Fèvre M, Rousseau B, Durrieu S, Teichmann M, Coindre JM, Lartigue L, Chibon F. Fusion-mediated chromosomal instability promotes aneuploidy patterns that resemble human tumors. Oncogene. 2019 Aug;38(33):6083-6094. doi: 10.1038/s41388-019-0859-6. Epub 2019 Jul 3. PMID:31270395

5. Lesluyes T, Baud J, Pérot G, Charon-Barra C, You A, Valo I, Bazille C, Mishellany F, Leroux A, Renard-Oldrini S, Terrier P, Le Cesne A, Laé M, Piperno-Neumann S, Bonvalot S, Neuville A, Collin F, Maingon P, Coindre JM, Chibon F. Genomic and transcriptomic comparison of post-radiation versus sporadic sarcomas. Mod Pathol. 2019 Jun 26. doi: 10.1038/s41379-019-0300-2. PMID:31243333

TEAM 20 Molecular dynamics of lymphocyte interactions

TEAM ACCREDITED BY THE LIGUE CONTRE LE CANCER

Team leader: Dr Salvatore Valitutti

Keywords: T-cell activation, T-cell antigen receptor, immunological synapse, cytotoxic T-cells, human immunology, tumor immunology, cell-mediated cytotoxicity, live-cell imaging, interdisciplinary research
Funding sources: Ligue Nationale Contre le Cancer, ANR - LabEx Toucan, Occitanie Regional Council, Cancéropôle Grand Sud-Ouest, Fondation Toulouse Cancer Santé, F. Hoffmann-La Roche, Laboratoires Pierre Fabre
Research theme: The four major lines of research pursued by the team in 2019 involved: i) investigating why the ability of human cytotoxic T-cells (CTCs) to kill target tumor cells varies; ii) studying ex vivo the phenotype and function of CTCs from patients with chronic lymphoid leukemia and seeking a correlation between the "functional strength" of each patient's CTCs and progression of the disease (1); iii) determining the molecular mechanisms that allow aggressive tumors such as melanomas to resist attacks by CTCs at the lytic synapse level; and iv) developing mathematical models to mimic the interactions between CTCs and target tumor cells (2).

In 2019, as part of LabEx Toucan-2, the team strengthened its capabilities by recruiting a data-processing expert to analyze, quantify and interpret the results of imaging studies of the interaction between CTCs and target tumor cells, both ex vivo and in tissue samples from patients. It also patented two methods for studying the efficacy of CTCs in infiltrating tumors. These methods can be used to better stratify patients receiving immunotherapy.

Major publications in 2019

1. Gonnord P, Costa M, Abreu A, Peres M, Ysebaert L, Gadat S, Valitutti S. Multiparametric analysis of CD8+ T cell compartment phenotype in chronic lymphocytic leukemia reveals a signature associated with progression towards therapy. **Oncoimmunology**. 2019 Feb 7;8(4):e1570774. doi: 10.1080/2162402X.2019.1570774. eCollection 2019. PMID:30906665
2. Khazen R, Müller S, Lafouresse F, Valitutti S, Cussat-Blanc S. Sequential adjustment of cytotoxic T lymphocyte densities improves efficacy in controlling tumor growth. **Sci Rep**. 2019 Aug 23;9(1):12308. doi: 10.1038/s41598-019-48711-2. PMID:31444380
3. Gonnord P, Valitutti S, Costa M, Ysebaert L, Gadat S. Procédé pour prédire le besoin de thérapie pour des patients souffrant de leucémie lymphoïde chronique. **Brevet WO2019149736 A1**, 2019

TEAM 21 Epigenomics and network modeling applied to studies of heterogeneity in oncoimmunology

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

Team leader: Dr Vera Pancaldi

Keywords: Bioinformatics, epigenomics, network theory, chromatin architecture, mathematical models, heterogeneity, cancer, oncoimmunology, pancreatic adenocarcinoma, machine learning
Funding sources: CRCT Chair of Bioinformatics in Oncology (Fondation Toulouse Cancer Santé, Institut de Recherche Pierre Fabre, Inserm)
Research theme: The team applies bioinformatics methods to oncoimmunology in order to ascertain how variability in patient profiles (transcriptome and immune cell characteristics) impacts responses to treatment, including but not limited to immunotherapies. For example, it has developed a method for determining the molecular bases of comorbidities between different conditions and plans to study the relationship between disorders of the immune system and the risk of developing cancer.
Another project will use innovative methods derived from network theory to investigate ways of linking the variability and plasticity of an individual's immune cells to the epigenome of these cells (methylation profiles, histone modifications, genome architecture). These methods, which combine agent-based and Boolean models with machine learning approaches, can also be used to characterize interactions between different types of cells in the tumor microenvironment, particularly in pancreatic adenocarcinomas. This will enable the team to move beyond quantifying different types of cells to perform in-silico simulations of the tumor microenvironment. The team is also at the heart of LungPredict, a collaborative project between the CRCT, Toulouse University Hospital and the Pierre Fabre Research Institute, whose goal is to enable the personalization of treatment and optimization of immunotherapy for patients with lung cancer. Achieving this goal will require collecting and analyzing multidimensional data (gene expression, multiplex immunohistochemistry, mutations and clinical files) from large numbers of lung cancer patients. A pilot phase (80 patients with all data analyzed), completed at the end of 2019, provided an invaluable database for testing the team's methods.

Major publications in 2019

1. Fores Martos J, Catala Lopez F, Sanchez Valle J, Ibanez Garikano K, Tejero H, Palma Gaudiel H, Climent Bataller J, Pancaldi V, Fananas Saura L, Arango Lopez C, Parellada M, Baudot A, Vogt D, Rubenstein J, Valencia A, Tabares Seisdedos R. Transcriptomic metaanalyses of autistic brains reveals shared gene expression and biological pathway abnormalities with cancer. **Mol Autism**. 2019 Apr 8;10:17. doi: 10.1186/s13229-019-0262-8. eCollection 2019. PMID:31007884
2. Ben Zouari Y, Molitor AM, Sikorska N, Pancaldi V, Tom Sexton T. ChiCMaxima: a robust and simple pipeline for detection and visualization of chromatin looping in Capture Hi-C. **Genome Biol**. 2019 May 22;20(1):102. doi: 10.1186/s13059-019-1706-3. PMID:31118054.
3. Jodkowska K*, Pancaldi V* (co-first), Almeida R, Rigau M, Graña-Castro O, Fernández-Justel JM, Rodríguez-Acebes S, Rubio-Camarillo M, Carrillo-de Santa Pau E, Pisano D, Al-Shahrour F, Valencia A, Gómez M, Méndez J. Three-dimensional connectivity and chromatin environment mediate the activation efficiency of mammalian DNA replication origins. **BioRxiv** 644971. doi.org/10.1101/644971.
4. Greco A, Sanchez Valle J, Pancaldi V, Baudot A, Barillot E, Caselle M, Valencia A, Zinovyev A, Cantini L. Molecular Inverse Comorbidity between Alzheimer's Disease and Lung Cancer: New Insights from Matrix Factorization. **Int J Mol Sci**. 2019 Jun 26;20(13). pii: E3114. doi: 10.3390/ijms20133114. PMID: 31247897

Technology Cluster

Manager: Dr Frédéric Lopez

The Technology Cluster 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.

Focus 2019

- Installation of an XRad Smart Plus (Jack) small animal research irradiator.
- Development of software to analyze single-cell signatures across scRNA-seq datasets.
  Pont F, Tosolini M, Fournié JJ. Single-Cell Signature Explorer for comprehensive visualization of single cell signatures across scRNA-seq datasets. Nucleic Acids Res. 2019 Dec 2;47(21):e133. doi: 10.1093/nar/gkz601. PMID:31294801

New equipment 2019:

- Purchase of an Incucyte S3 (Sartorius), with funding from Inserm's "Plan Cancer"
- Purchase, from the Technology Cluster's own budget, of a gentleMACS Octo Dissociator (Miltenyii) and a Chemidoc (Bio-Rad) gel imaging system.

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

TECHNOLOGY CLUSTER

- 9 technical units / 900 m²
- 17 staff (equiv. 15 full-time posts)
- **Total budget: €600,000**

Iso 9001- 2015
NFX 50-900

CONSULTANCY / ANALYSIS

- Experiment design
- Data analysis
- Analysis reports

TRAINING AND ASSISTANCE

- Open-access
- Reservation

R&D

- Collaborative projects
- Development of new methods

2019

103 projects
73 training sessions
117 open-access users
30 papers/years

98 % satisfaction index

Research-healthcare interconnections

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 following diagram shows the main OCC with which each CRCT team collaborates. Most teams have connections with several OCCs.

Main CRCT-IUCT-O collaborations

TEAM 13
H. AVET-LOISEAU / L.MARTINET
TEAM 16
E. DELABESSE
TEAM 9
J-J. FOURNIÉ
TEAM 7
P. BROUSSET / F.MEGGETTO
TEAM 18
J-E. SARRY
TEAM 8
S. MANENTI

HEMATOLOGY

TEAM 14
E. CHATELUT
TEAM 12
M. POIROT /
S. SILVENTE-POIROT

BREAST CANCERS

TEAM 3
G. FAVRE
TEAM 21
V. PANCALDI
TEAM 20
S. VALITUTTI

THORACIC CANCERS

TEAM 1
M. AYYOUB /
J-P. DELORD

GYNECOLOGICAL CANCERS

TEAM 5
S. MILLEVOI

HEAD & NECK CANCERS

TEAM 10
P. CORDELIER
TEAM 17
J. GUILLERMET-GUIBERT
TEAM 6
S. PYRONNET / C. BOUSQUET

DIGESTIVE CANCERS

TEAM 19
F. CHIBON

SARCOMAS

TEAM 4
T.LEVADE /
N. ANDRIEU

SKIN CANCERS

TEAM 11
E. MOYAL /
C. TOULAS

NEURO-ONCOLOGY

TEAM 2
M-J. PILLAIRE

ONCOGENETICS

III

PATIENT CARE AND CLINICAL RESEARCH

Key figures

35,423 patients treated in 2019 (+2.98% compared with 2018) including **10,283** new patients who came to the technical centers or the consultation, radiotherapy or hospitalization departments (+1.69% compared with 2018)

3,048 patients received oral therapies (+14% compared with 2018)

107,899 hospital stays (+2.47% compared with 2018), including 58,107 radiotherapy sessions

187 transplants, including **72** allogenic transplants and **125** autologous transplants (hematology and solid tumors)

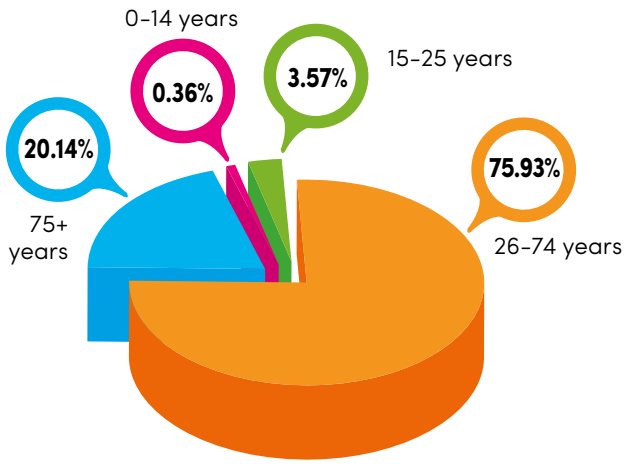
8 patients treated with CAR-T cells

79,6 % outpatients in the hospitalization departments

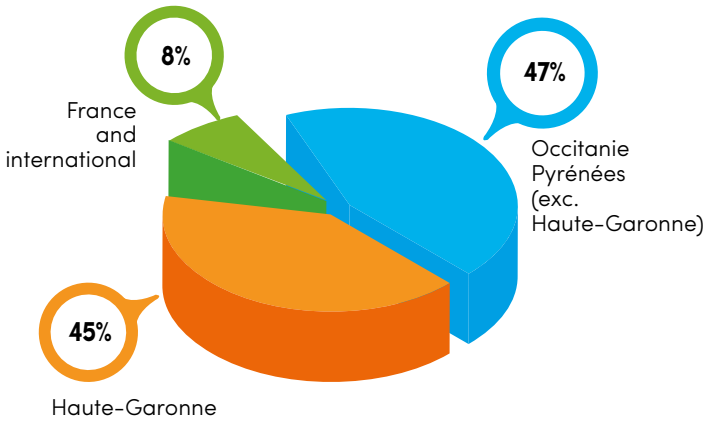
43,2 % men - **56,8 %** women

201 clinical trials included patients in 2019
1,651 IUCT-Oncopole patients included in clinical trials, that is 16% of patients (active files)
56.21 % of trials were early phase trials

Distribution by age group



Géographical origin of patients



A personalized care pathway for each patient

The IUCT-Oncopole brings together all the disciplines needed to detect, treat and monitor cancer, and its state-of-the-art technical facilities ensure patients have access to the latest advances in diagnosis and treatment. Moreover, the IUCT-Oncopole's multi-disciplinary approach, centered round weekly multidisciplinary team (MDT) meetings, guarantees that every patient receives the best possible care and benefits from a personalized and innovative treatment program.

Areas to promote patient well-being

A convalescence/wellness garden has been laid out within the IUCT-Oncopole's grounds. With its harmonious arrangement of flowerbeds, herb gardens and vegetable patches, chosen by experts from the Laboratoire Pierre Fabre's Botanical Conservatory, it is both an area for therapeutic reeducation (with six pieces of apparatus) and a pleasant place in which to relax. Inside, the IUCT-Oncopole's reception hall includes areas where patients can rest and relax while waiting for their appointments.

Integrated and personalized supportive care

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

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. In 2019 Stade Toulousain Rugby Club joined the program by providing sports therapy sessions at the Ernest-Wallon Stadium. 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, as part of a "sport and health" protocol promoted by the French Rugby Federation.

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 each patient's overall health (possibility of multiple pathologies), their autonomy and their family situation. The Geriatric Oncology OCC — working within the Geriatric Oncology Coordination Unit set up in conjunction with Toulouse University Hospital and the Onco-Occitanie network — takes into account all these parameters when drawing up treatment programs, in order to find the best compromise between efficacy and quality of life.

"Health Partnerships"

The IUCT-Oncopole's healthcare staff, associations and users work together to continually improve the quality of patient care. Thus, care provision is now viewed as a form of "healthcare partnership", based on co-leadership, co-construction and co-responsibility, in which the hospital staff's expertise is combined with feedback from patients and their relatives.

A Cancerology Transversal Therapeutic Patient Education Unit

In 2019 Occitanie Regional Health Agency named the IUCT-Oncopole as the "sponsor and guarantor of the Cancerology Transversal Therapeutic Patient Education Unit for the Occitanie Region". Coordinated by E. Arfé and Dr N. Caunes-Hilary, the unit's main objectives are to develop therapeutic patient education (TPE) in Occitanie and to finalize the creation of a center for patients receiving oral chemotherapy, a project the IUCT-Oncopole launched in 2015. In 2019 more than 700 patients attended therapeutic education group sessions as part of their cancer care pathway and three approved cancer treatment establishments benefitted from the IUCT-Oncopole's expertise in TPE.

A patient expert was hired in May 2019 as a "technician to promote therapeutic patient education". The successful candidate, a graduate of the "Patients University" at UPMC Sorbonne-Université, is in charge of extending the "Cancer Oral Therapy: I can manage" TPE program across the Occitanie-Est Region.

Two new TPE programs for transplants

2019 saw the launch of two new TPE programs —a pre-transplant program ("3, 2, 1... Prêt? Greffe!") and a post-transplant program ("Le MAG (MonAlloGreffe): A La Une !")— to help patients receiving hematopoietic stem-cell transplants. Both programs were created under the impetus of Dr A. Huynh.

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 in which they can receive patients and their families has been set up at the heart of the IUCT-Oncopole. Some of these charities provide specialist services. For example, the Palliative Care Association (ASP) offers palliative support to patients and their caregivers, while the Brain Tumor Research Association (ARTC) helps families look after patients at home.

Several additional associations joined the IUCT-Oncopole's partners in 2019, including 20 ans 1 Projet (20 years old, 1 project), Hôpital Sourire (Hospital Smile) and Un maillot pour la vie (A Team-shirt for Life). Consequently, 20 associations now work alongside the IUCT-Oncopole's healthcare professionals to provide patients with help and advice.

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.

The Users' Project

2019 saw the first steps towards creating a Users' Project for the IUCT-O, as allowed for under the decree of June 1, 2016 relating to healthcare users' rights committees. Users' Projects are a way for healthcare facilities to identify and meet users' needs and expectations, as expressed by patients and caregivers themselves. In line with the decree, the IUCT-Oncopole, through the Institut Claudius Regaud, made it possible for patients, caregivers, patients' representatives and patients' associations to come together with healthcare profes-

sionals of every category to co-construct a project that will benefit all IUCT-Oncopole users. The 2019-2020 Users' Project upholds the hospital's guiding principles in terms of the quality and safety of patient care and treatment. Inspired by the values, principles and key concepts of the IUCT-Oncopole's overall, research and healthcare missions, it will enable users to exercise their rights and ensure they are respected. The Users' Project also reflects the commitment made by all levels of the IUCT-Oncopole's management (Director General, Medical Commission, Operational Management, Healthcare Departments) and users' representatives to place patients and caregivers at the heart of healthcare practices. However, the Users' Project not only allows users to exert their rights, it will also help the IUCT-O's healthcare professionals manage potentially complex processes.

The 2019-2020 Users' Project has three main objectives:

- To organize the discharge procedure so that each patient is given a personalized, interactive guide, drawn up by the healthcare team in consultation with the patient, containing information and advice to facilitate the return home and help avoid possible difficulties.
- To foster the well-being of users and hospital staff all along the care pathway by promoting the services provided by the Supportive Care OCC via a partnership between patients, caregivers and healthcare professionals.
- To help create closer partnerships between patients, caregivers and health professionals from the start of a patient's care pathway.

Innovation at the heart of patient care

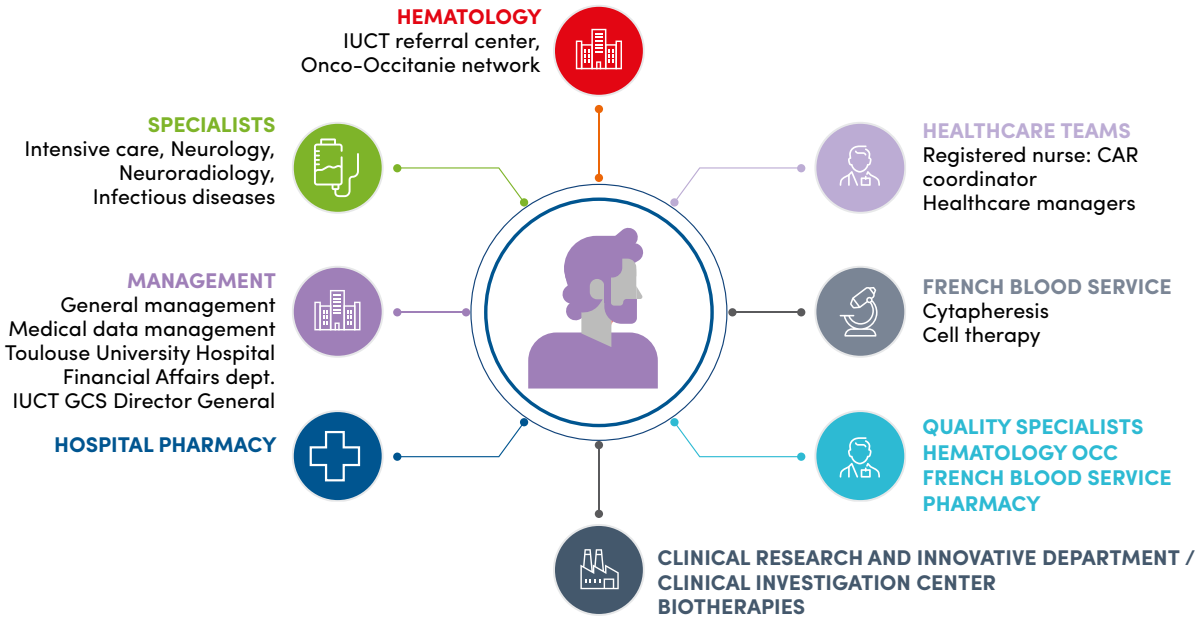
Innovative therapies

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

The close ties between the hospital's clinicians, supported by the Clinical Research and Innovation Department, and the CRCT's research teams, combined with the procedures introduced by the Clinical Trials Office to achieve INCa CLIP² early-phase trials accreditation, means that it takes less than six months for a laboratory discovery to be translated into a clinical trial at the IUCT-Oncopole. The IUCT-Oncopole's clinicians and paramedical staff also design their own therapeutic research projects to evaluate innovative practices. Moreover, the teams work together to create the best possible conditions for developing innovative techniques.

CAR-T therapy comes to the IUCT-Oncopole

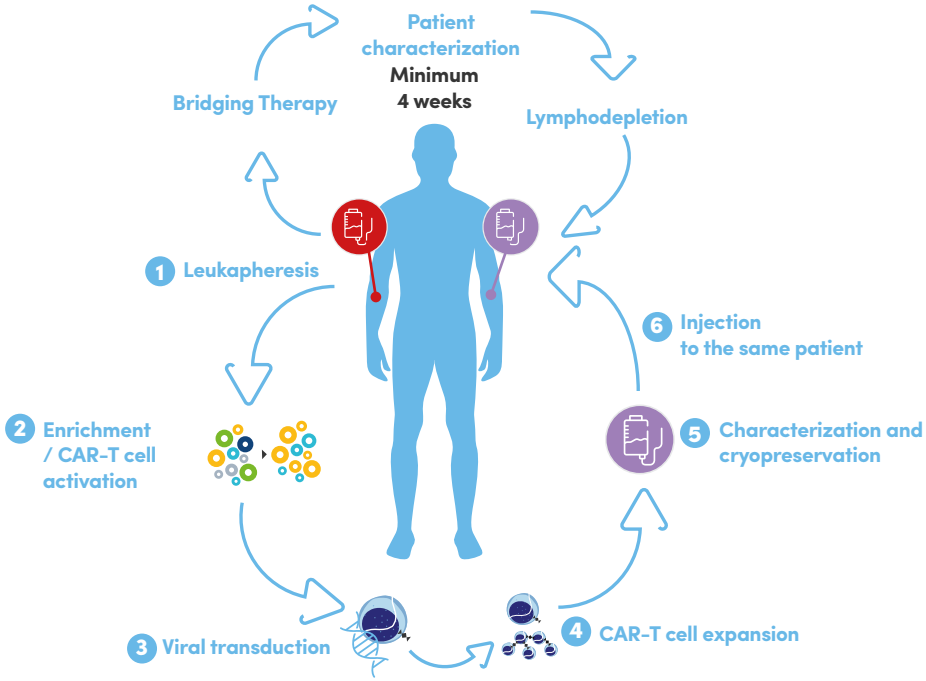
The first two Gilead and Novartis accreditations were obtained in 2019 thanks to wide-ranging collaborations steered by Dr P. Bories of the Onco-Occitanie network. Within the IUCT-Oncopole, these accreditations most directly concerned the Hematology OCC (contact: Dr A. Huynh), where patients are treated; the Intensive and Continuing Care Department (CAR-T cell contact: Dr M. Picart) and the Neuro-oncology OCC (CAR-T cell toxicity contact: Dr D. Larrieu-Ciron), for managing toxicities; and the Pharmacy (contact: Dr A. Grand), Technical Services Department (D. Fasano & J-C. Godard) and Biomedical Engineering Department (L. Panassié), for installing a specific cryopreservation chamber. The French Blood Service's cytapheresis and cell therapy teams are also involved in the process, because 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 brain MRI scans and ECGs are interpreted immediately in the case of toxicities. The first patient at the IUCT-Oncopole to receive CAR-T cell therapy was treated on July 30, 2019. Seven more patients received this innovative therapy between September and December 2019.



The teams involved in providing CAR-T cell therapy

Principles of CAR-T cell therapy

T lymphocytes are a type of white blood cell whose main role is to destroy malignant cells and cells infected by a virus or a bacterium. Cancer weakens T cells, thereby allowing tumors to develop more easily. CAR-T cell therapy works by increasing both the potency and quantity of T cells. To do this, T cells are harvested from a patient and genetically modified in vitro in order to produce an artificial T-cell receptor, known as a chimeric antigen receptor (CAR), capable of recognizing a tumor antigen. After several processing stages, these T cells are reinjected into the donor patient, who thereby receives a form of personalized immunotherapy.



From Roberts ZJ, et al. Leuk Lymphoma 2018; 59:1785-1796.
Better M, et al. Cell Gene Ther Insight 2018; 4:173-186/

Digital innovations for patient home monitoring

The increase in the number of patients who receive their treatment as outpatients and/or as oral therapies has made it necessary to develop new ways of monitoring patients at home. To this end, 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 CoAC TCO for solid tumors; AMA1, AMATO and AMA-AC for hematology).

« Mon E-suivi IUCT-Oncopole », a web app for patients

The "Mon E-suivi IUCT Oncopole" web app, developed in association with MHComm, was officially launched in 2019. Results of a pilot study of 35 outpatients carried out in 2018 (funded by INCa and coordinated by Dr A. Daboussi, PICTA) were extremely positive, as 96.7% of participants were satisfied with the system, 93% said it made them feel safer and 97% found it easy to use. The app includes seven different programs covering surgery, oncology and hematology outpatient pathways, as well as nutritional monitoring for radiotherapy patients.

A smartphone chatbot for older patients

In 2019, two years after introducing a telephone monitoring system for older cancer patients, the Geriatric Oncology OCC has improved and updated the system by creating a smartphone app in the form of a semi-automatic messaging system centered round a chatbot. Called Infinity®, the new app will improve telephone monitoring by reducing the number of unnecessary calls. Results of a study evaluating the app's effectiveness and its acceptability among its target users were very positive.

Clinical research

Member of numerous INCa clinical research networks

The IUCT-Oncopole, which was one of the first three members of the CLIP² network of INCa-accredited early phase trials centers (coordinator: Prof. J-P. Delord), saw its accreditation renewed for five years in 2019. In addition, the IUCT-Oncopole (through the Institut Claudius Regaud) has joined forces with Bordeaux University Hospital, the Institut Bergonié and 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 is 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 for which there is as yet no therapeutic standard. The network's 27 members include 16 Comprehensive Cancer Centers. In 2019 Prof. J-P. Delord and Dr C. Gomez Roca hosted OncoDistinct's 8th annual congress at the IUCT-Oncopole.

Co-creator of the association SCOPP

In 2019 Prof. J-P Delord co-created the association SCOPP – Academic Association for Developing Early-Phase Onco-Hematology Trials in France - in collaboration with Dr C. Massard (Institut Gustave Roussy), Prof. J-Y. Blay (Centre Léon Bérard/President of Unicancer), Prof. G. Salles (Lyon University Hospital), Prof. J-P. Spano (Pitié Salpêtrière), Prof. A. Italiano (Institut Bergonié) and F. Barlesi (AP-HM/Institut Gustave Roussy). SCOPP's objective is to ensure patients receive rapid access to new drugs by bringing together clinicians who specialize in early-phase trials and by promoting such trails in discussions with decision-makers, corporations and patients' associations. The launch conference was held in Paris in November 2019.

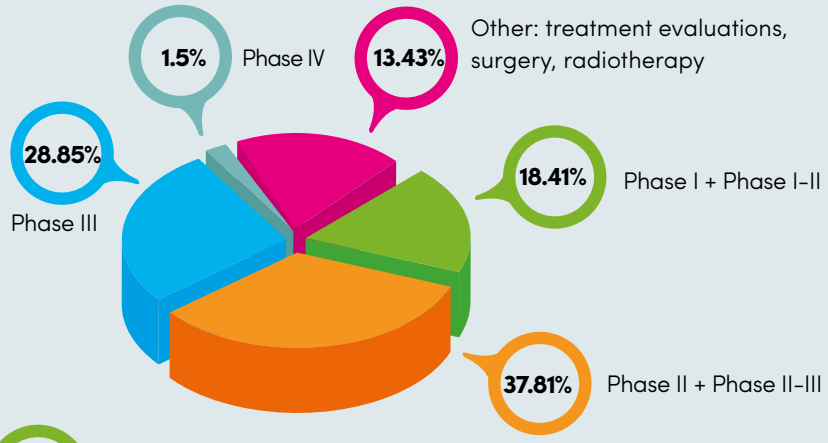
Pioneering quality assurance procedures for research

• In 2013, the Institut Claudius Regaud became France's first cancer clinical research establishment to obtain ISO 9001 certification, alongside the Institut Paoli Calmettes (certified by Veritas). In 2019 this certification was extended to the Methodology & Biostatistics Unit, which helps research teams design methodologies and process data. The new certification is entitled ISO 9001:2015 "Design and Realization of Clinical and Translational Studies. Methodological Research in Cancerology".
• Toulouse University Hospital was France's first university hospital to obtain ISO 9001 certification for its Research and Innovation Department. Its certification, obtained in 2015, covers "project management within Toulouse University Hospital's Research and Innovation Department: promotion and partnerships". France's standards organization (AFNOR) granted the certification after auditing the department's internal promotion, partnerships, knowledge sharing and project implementation procedures and the support processes involved in managing research projects..

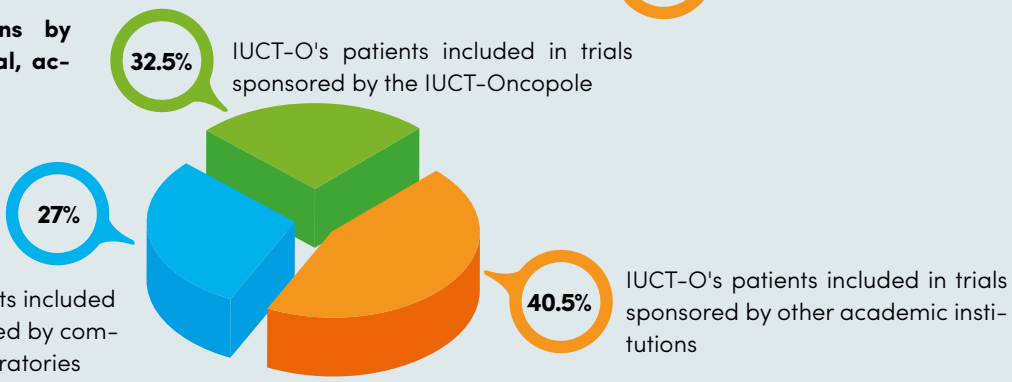
Clinical research indicators

201 clinical trials included patients in 2019, **31** of which are promoted by IUCT-Oncopole
1,928 patients, including **1,651 IUCT-Oncopole patients** (**16%** of active files), included in a clinical trial in 2019
56.21% of trials were early-phase trials
15.4% of clinical trials that included patients in 2019 were sponsored by

Trials that included patients in 2019: proportion by trial phase



Percentage of inclusions by sponsor type (commercial, academic, etc.)



Methodological research to optimize clinical trials

As well as providing methodological support to the Clinical Trials Office, the Biostatistics Unit, coordinated by T. Filleron, researches ways of improving the statistical processing of therapeutic trials. In 2019 the unit worked with Toulouse School of Economics on projects to optimize the duration and frequency of post-therapeutic monitoring and to optimize methods for selecting variables for high dimension datasets. In addition, to further the development of personalized medicine, the unit is devising clinical trial methodologies that can evolve as a function of the knowledge produced. Heterogeneity in small populations is another theme the unit is investigating, most notably in collaboration with the Geriatric Oncology OCC. 2019 was a special year for the unit because it hosted the CLCC/EPICLIN conference, which combined the CLCC's (Center for the Fight Against Cancer) Statisticians' Workshop and the French Clinical Epidemiology Conference. 220 participants from across France attended the conference.

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) and OTX (Novartis). The IUCT-Oncopole is also the first French center to sign a Master Agreement with the imCore network (Genentech). This agreement will enable the institute to launch the IUCTO-ImCORE "THALYES" 2020-22 project, which will be steered by Prof. L. Ysebaert and carried out in collaboration with CRCT team 9 (coordinator: Prof. C. Laurent). The project will use biopsies from lymphoma patients to produce 3D models that can be used to test drugs with the aim of offering patients truly personalized treatments in the very near future.
2019 also saw the signing of a new multi-year agreement, called "Alliance Oncopole", with the Pierre Fabre Research Institute. Its aim is to boost innovation in cancer treatment in order to develop alternative personalized therapies.
Finally, transfer agreements have been signed with a number of commercial companies, giving them limited access to datasets resulting from clinical trials.

Selected research projects

In 2019 the IUCT-Oncopole signed the "Alliance Oncopole" multi-year agreement with the Pierre Fabre Research Institute and the IUCT Larrey. Its aim is to develop new personalized therapies. Several projects have already been launched:

LUNG Predict sponsored by Prof. J. Mazières / G. Favre aims to establish a molecular map of lung cancers. A pilot phase, begun in February 2019, will define processes and methodologies for conducting multi-parameter analyses of patients' tumors. Phase 2, planned for 2020, will apply and extend the molecular characterization of tumors to more patients. In the future, it may be possible to draw up similar maps for other types of tumor, such as melanomas, bowel and rectal cancer and breast cancer.

- Two projects in the Pierre Fabre Research Institute's R&D portfolio — investigations of an antibody conjugated with a cytotoxic drug (ADC), currently the subject of a phase I clinical trial, and of a new type of immunotherapy, which is in the pre-clinical trial phase — will be complemented by a new project to identify the most relevant therapeutic indications and the patient profiles most likely to respond to the treatment.
- Another project is being designed to develop an antibody capable of neutralizing certain immunosuppressive cells (macrophages) that contribute to cancer growth.

Numerous projects were awarded funding under national competitive grant schemes in 2019. Here is a selection:

« **SI2GMA**- Integrated bio-imaging markers of response to hypofractionnated stereotatic irradiation and anti-PDL1 Durvulumab combination in recurrent glioblastoma", coordinated by Prof. E. Moyal. Funded under the Fondation ARC's first competitive grant scheme: "SIGN'IT: Signatures in immunotherapy"
This project builds on data collected during the STERIMGLI clinical trial, also coordinated by Prof. Moyal, which compared tolerance to and efficacy of hypo-fractionated stereotactic radiation therapy administered alone and combined with immunotherapy (anti-PDL1). In order to identify a "signature" that can be used to predict responses to combined immunotherapy/radiation therapy, the research team will collect and compare scan, genetic, and cellular biology data from 50 patients. Multimodal MRIs will be carried out every two months to study tumor morphology and activity (vascularization and metabolism). Blood samples taken before and during treatment will be analyzed to ascertain their protein composition (proteome), detect the exosomes that enable cancer cells to communicate remotely with other cells, and monitor the characteristics and activity of blood lymphocytes. The team will also analyze biopsies taken during diagnoses and tumor samples taken during surgery in order to collect information about the protein PD-L1 and to determine the number of DNA mutations in the cancer cells, an indicator that has already been correlated with response to immunotherapy in other cancers.

« **EPOP-Sarcoma** – Efficacy of pre-operative rehabilitation in patients with limb sarcomas" sponsored by Dr D. Gangloff. Funded by the Ligue Nationale Contre le Cancer.
Most limb sarcomas are generally large tumors that can be treated only by invasive surgery, such as removing muscle, bone and sometimes vessels and nerves inside or close to the tumor. The main goal of the EPOP-Sarcoma phase 2 study is to evaluate the efficacy of pre-operative rehabilitation in patients with limb sarcomas. EPOP-Sarcoma was inspired by published data on pre-operative rehabilitation in other types of cancer and aims to improve the recovery of limb function and increase patient autonomy, a goal that is made even more important by the young age of many limb sarcoma patients.

« **SAMHY Sarcome** – Circulating hybrid sarcomatoid cells/macrophages in sarcomas?", sponsored by Dr V. Thibaud in collaboration with CRCT team 19 (OncoSarc, coordinator: Dr F. Chibon). Funded by the Fondation ARC
Several studies have shown that the cancer cell-immune cell (macrophage) fusion mechanism can promote the metastatic spread of malignant cells by enabling them to acquire the plasticity and migration properties inherent to immune cells. According to recent studies, these circulating hybrid cells may be responsible for poor outcomes in some malignant pathologies.
Analyses of tumor samples taken under the International Cancer Genome Consortium's leiomyosarcoma program revealed the presence of hybrid macrophage/cancer cells, suggesting that this fusion mechanism may be relevant to sarcoma oncogenesis.
The SAMHY Sarcome pilot study will pursue this research theme by looking for circulating hybrid macrophage/cancer cells in the blood of sarcoma patients and investigating possible clinical implications.

« **TEC ORL** - Phase II randomized comparison to assess the value of Qutenza when treating patients in remission from head and neck cancers and experiencing chronic

neuropathic pain", sponsored by Dr A. Boden. Funded by a PHRCI GIRCI SOHO grant.
According to a recent study, more than 50% of patients in remission from head and neck cancers who suffer from chronic neuropathic pain in the cervicofacial area take an opiate-based treatment. Given the side effects of these drugs, there is a need for alternative painkillers. TEC ORL has been designed to address this need by comparing patient tolerance to and the effectiveness of Qutenza patches (capsaicin) compared with amitriptyline, the standard neuropathic treatment for this type of pain.

« **OvaSarc** – the CINSARC genetic signature as a predictor of the resectability of high-grade serous ovarian adenocarcinomas", sponsored by Dr S. Bétrian and Dr T. Valentin. Funded by a GIRCI SOHO APIK grant.
In 2010, Dr F. Chibon and his team used the expression profile of 67 genes involved in mitotic control and chromosome integrity to identify a molecular signature, baptized CINSARC, in a cohort of patients with soft-tissue sarcomas. They showed that this transcriptome signature was an independent prognostic factor in several types of soft-tissue sarcoma, and more discriminant than histological classification, the classic and most widely used prognostic factor.
OvaSarc's main objective is to evaluate the CINSARC signature's reliability in predicting surgical resectability after neodjuvant chemotherapy in patients with high-grade ovarian serous adenocarcinomas.

In addition to clinical trials and collaborations with the CRCT, members of the OCCs and the IUCT-Oncopole's medico-technical departments conduct research projects on a wide variety of themes. A few examples are given below:

Liquid biopsies:
The Oncology Medical Biology Laboratory's Prospective Biology Unit (coordinators: Prof. G. Favre and Dr A. Pradines) 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 research projects directly linked to the CRCT. Working in collaboration with CRCT team 3 (coordinator: Prof. G. Favre), the unit conducts its own projects aimed at developing new circulating biological markers for diagnosis, prognosis, longitudinal monitoring and therapeutic response prediction: circulating nucleic acids (RNA, then DNA), circulating tumor cells and, more recently, circulating immune cells. It also has the expertise needed to carry out a wide range of circulating biomarker analyses for clinical trials.
Since 2019 the Prospective Biology Unit 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 safety and effectiveness of a combined palbociclib-hormone therapy treatment for patients with metastatic breast cancer. The unit will also take part in a translational study related to PADA-1 and aimed at understanding late resistance mechanisms. This study, called YODA, is sponsored by Prof. F. Clément-Bidard (Institut Curie) and will begin in 2020, thanks to PHRC funding. Finally, the unit is a member of the LUNG-RESIST project to understand and prevent adaptive resistance to EGFR tyrosine-kinase inhibitors in lung cancer. Launched in 2019 by Prof. J. Mazières (Thoracic Cancers OCC/CRCT team 3), LUNG-RESIST is supported by the DGOS and the INCa (PRT-K grant).
One of the Prospective Biology Unit's objectives for 2020 is to expand its use of next-generation sequencing to analyze circulating tumor DNA.

Pharmacokinetics & pharmacodynamics
2019 saw a large increase in the number of molecules routinely dosed by the Oncology Medical Biology Laboratory's Pharmacology Unit (coordinator: Prof. E. Chatelut), mostly because it began monitoring oral drugs such as tyrosine kinase inhibitors. The unit also conducted several drug research projects (immunity checkpoint inhibitors, tyrosine kinase inhibitors) in 2019 and began moving towards the dosing of metabolites (in order to differentiate between compliance issues and "hyper-metabolization").
Dr F. Thomas is responsible for developing pharmacodynamics research projects (metabolization and aromatases). 2019 saw the publication of the results of the PHACS study (Pharmacokinetics of tamoxifen and anti-aromatases, correlation with pharmacogenetic characteristics), which included more than 2,000 patients.
In addition, the Pharmacology Unit was one of the first academic teams to do population pharmacokinetics and is now applying this methodology to the use of radioactive tracers in theranostics, an innovative approach to cancer treatment whose pharmacological component had been largely overlooked. Several research projects in this area were launched in 2019, one of which was granted PHRC funding.

Clinical Immunological monitoring
The Immune-monitoring Unit (coordinator: Prof. M. Ayyoub) was created in 2017 to support work to develop immunotherapies by the IUCT-Oncopole's clinicians. The unit's main objective is to identify the biological parameters associated with clinical responses to immunotherapies. It is doing this by monitoring patients during immunotherapy clinical trials, including the CITHARE (Dr A. Modesto), BOOSTER Melanoma (Dr C. Gomez-Roca), SILK BM (Prof. E. Cohen-Jonathan Moyal) and STERIMGLI (Prof. E. Cohen-Jonathan Moyal) trials. The unit also runs its own trials in collaboration with CRCT team 1. MINER, for example, was launched in 2018 by Prof. J-P. Delord and Prof. M. Ayyoub, in collaboration with Prof. J. Mazières, to monitor immunological resistance mechanisms and response biomarkers in patients with different types of cancer (lung, bladder, head and neck, etc.) treated

by immunotherapy. In addition, 2019 saw the launch of DECIdE, sponsored by Dr A. Martinez and Prof. M. Ayyoub, which will analyze spontaneous immune responses to tumors in several types of cancer (ovarian, cervical, head and neck, etc.) before any therapy begins, in order to ascertain which types of tumor are likely to respond to immunotherapy. All of these trials and studies are supported by the imCORE network, the MSDAVENIR foundation, AstraZeneca and Bristol-Myers Squibb.

Artificial intelligence

• At the end of 2019 Prof. J-P. Delord, in partnership with MH-Comm, Alcimed and the CEA, launched an artificial intelligence (AI) project to develop a demonstrator capable of realistically simulating the supervision of a patient with breast cancer receiving home care.

• Dr S. Kanoun is looking at the perspectives AI offers for medical imaging. In 2019 he launched a program to train a computer to recognize tumors from PET images. A first stage involving hand-segmented images from 200 patients achieved 75% pixel recognition. The learning program will continue in 2020 by increasing the number of patients and exploring an alternative technique involving recognizing tumors by comparing them with PET images with no tumor. Thanks to funding from the CALYM consortium (Institut Carnot), a project to automatically calculate tumor volumes will be launched and integrated into the GaelO platform's clinical trials workflow. GaelO is an academic image management platform that was designed in 2019 by Dr S. Kanoun, in collaboration with the Lymphoma Study Association, Toulouse University Hospital and the Institut Claudius Regaud, to securely collect and share medical images used in clinical trials.

• The renewal of LabEx TOUCAN for five years (2020-2024 – coordinator: Prof. P. Brousset) will enable the program to develop several AI projects, including:
- Use of non-supervised machine learning to characterize grade 2 breast cancers, in collaboration with Unicancer and Thalès Services (coordinated by Dr C. Franchet).
- Analysis of histological images to predict the characteristics of large-cell B lymphomas (sponsored by Prof. C. Laurent and Prof. L. Ysebaert).
In addition, CRCT team 20 (coordinator: Dr S. Valitutti), in collaboration with the Pathology Department's Imaging Unit, has launched a project that will use machine learning to develop a computer method for analyzing complex functional microscopy images (multiplex immunofluorescence).
• Another project, sponsored by Dr C. Franchet (Breast Cancer OCC), was awarded funding from the first competitive grant scheme run jointly by the Inter-Ministerial Directorate for Digital Technology (Dinum) and the Inter-Ministerial Directorate for Modernizing Public Administration (DITP). Its aim is to facilitate decision-making in post-operative MDT meetings by producing a tool capable of extracting essential medical information from pathology reports and presenting it in an appropriate form. Such a tool would reduce administrative work, eliminate mistakes when copying data and enable these data to be used in research. Phase 1, completed in 2019, involved creating a tool for annotating reports and developing the first text mining algorithms. The project will continue through 2020.

• The Medical Physics (especially 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 that specializes in deep learning. One such project aims to create an automatic tissue contouring tool for radiotherapy. In addition, Dr J. Khalifa and Dr C. Massabeau are looking into ways of improving 4D scanner images.
• Finally, 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

A collaboration in bioethics

In 2019 the Oncology Medical Biology Laboratory's Oncogenetics and Pharmacogenetics Units (coordinator: Dr C. Toulas) began a collaboration with Prof. B. Couderc (PU Biotechnologies and coordinator of the IUCT's Ethics Task Force), who is a member of Inserm UMR 1027 team 4 (BIOETHICS, coordinator: Dr E. Rial-Sebbag). As a result, Dr Toulas is coordinating two projects that will be launched in 2020. The first project aims to ensure that patients with a genetic predisposition to cancer receive the best possible information and adhere to their prescribed treatment, after giving informed consent, by improving communication between the different professions involved — prescribers of genetic analyses, geneticists (analyses), genetics counsellors, oncologists. Conducted under France's Plan Génomique 2025, the project is being funded by the Ligue Contre le Cancer. The second project, called "Sociological and ethical reflections on the use of palliative sedation at the end of life by professionals in the field of cancer treatment" was launched following work by the IUCT's ethics task force relating to the Claeys-Leonetti Act on the rights of patients at end of life. Funded by the ARC, it will be conducted by Dr A. Faya Roble (Inserm U1027 BIOETHICS team) and Prof. B. Couderc.

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 Pediatric Ependymoma Photons Protons and Imaging (PEPPI) study.

Collaborations with other research laboratories in Toulouse

Several IUCT-Oncopole technicians are members of non-CRCT research laboratories, which are exploring other avenues for fighting cancer:

• Prof. A. Laprie (Radiotherapy Department) is a member of the **Development and Validation of Biomarkers in MRI and Nuclear Medicine (DEVIN)** team, coordinated by Dr P. Peran, at Toulouse Neuro Imaging Center (ToNIC). DEVIN is a mixed Inserm U1214 and University of Toulouse III-Paul Sabatier research team that studies the brain and its main pathologies, including brain tumors, ballistics and cognition. It also coordinates the radiotherapy work package within the Multi-Regional Research On Brain – Optimized Therapy (MrROBOT) Program of Integrated Research Actions (PAIR), as well as the PAIR IMPALA prospective study. IMPALA will include 50 patients and 25 healthy volunteers in a project to determine the long-term impact of radiotherapy on the cerebellum and hippocampus of children, correlating radiation doses with metabolic and multifunctional multimodal MRI data and the results of advanced neuropsychological tests.

• Dr C. Vaysse (Surgery Department) is a member of the **Microenvironment, Cancer and Adipocytes** team (coordinator: Prof. C. Muller) at the Institute of Pharmacology and Structural Biology (UMR CNRS 5089 - IPBS), where she studies links between obesity and breast cancer. Since 2017 she has been investigating modifications to breast adipose tissues induced by obesity and the aggressiveness of breast cancer.

• Dr A. Dupret-Bories (Surgery Department) is an associate researcher at the **Inter-university Center for Materials Research and Engineering (CIRIMAT** - UMR CNRS INPT UPS 5085, director: Prof. C. Laurent). Several research projects are ongoing, notably a project to develop a biomaterial to treat mandibular osteoradionecrosis (Fondation des Gueules Cassées and Inter-CARNOT doctoral grant), and collaborations have been set up with companies (Rescoll, AnatomikModeling) to develop innovative products, especially by 3D printing. In addition, Dr A. Dupret-Bories coordinates the in vivo part of the TIPOLTI project (Institut Carnot MICA) to develop new osteosynthesis plates with a reduced risk of rejection.

• Dr P. Grosclaude has been seconded to UMR 1027's (Inserm – University of Toulouse III-Paul Sabatier) **team 5** - Embodiment, Social Inequalities, Life Course Epidemiology, Cancer and Chronic Diseases, Interventions, Methodology (EQUITY), coordinated by Dr C. Delpierre. She specializes in epidemiological studies of cancers.

• Dr S. Ken (Engineering and Medical Physics Department) is an associate researcher with the Computational Imaging and Vision (**MINDS,** coordinator: Dr A. Basarab) team at Toulouse Institute for Computer Research (IRIT), which develops advanced image analysis and interpretation tools.

Finally, the IUCT-Oncopole is a partner in a Horizon 2020 project:

MEDIRAD is a Horizon 2020 research project involving a consortium of 33 partners from 14 European countries. Coordinated by the European Institute for Biomedical Imaging Research (EIBIR, Austria), it consists of six interdependent work packages (WPs) aimed at exploring the effects of exposure to low doses of radioactivity. MEDIRAD's overall goal is to clarify the scientific bases underlying radiation protection in the field of medicine and improve clinical practice in order to eliminate the risks associated with repeated exposure to low doses of radiation (e.g., cardiovascular risks following radiotherapy treatment for breast cancer/long-term risks of tomography treatments in children and adolescents, etc.).
CRCT team 15 (leader: Dr M. Bardiès) provides expertise in dosimetry for WP3 (coordinator: Glenn Flux), which is investigating the doses of iodine 131 needed to treat thyroid cancers. The IUCT-Oncopole is the only French institution involved in the clinical study (coordinator: Prof. F. Courbon).

Member of the European MyPeBS study

The IUCT-Oncopole is one of 26 partners from five countries (France, Italy, Israel, Belgium and the United Kingdom) involved in MyPeBS, 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, aged between 40 and 70 years and who have never had breast cancer, will take part in the study (www.mypebs.eu).

Organ Coordination Committees

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

- Define personalized treatment pathways and ensure 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 in the way care is organized to the Patient Care Pathway Committee, without circumventing the decision-making channels defined by heads of departments or units;
- Conduct clinical and translational research in the OCC's field
- Help train experts and future professionals

The fifteen OCCs that work within the IUCT-Oncopole and the IUCT's other sites are listed below, together with their coordinators.

IUCT-O Organ Coordination Committees	
GYNECOLOGICAL CANCERS	Dr Laurence Gladieff
HEMATOLOGY	Prof. Christian Recher
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 Michel Rives
SARCOMAS	Dr Christine Chevreau
BREAST CANCERS	Prof. Florence Dalenc - Dr Eva Jouve - Dr 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 Pierre Graff-Cailleaud
DIGESTIVE CANCERS	Prof. Rosine Guimbaud
PEDIATRIC ONCOLOGY	Prof. Anne Laprie - Dr Marie-Pierre Castex
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.

IUCT-O OCC
BREAST CANCER

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

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	2,746 (+ 4.43%)
Surgery	1,427 (+ 5.78%)
Chemotherapy	1,179 (+ 0.34%)
Radiotherapy	992 (+ 1.64%)

45 physicians
35,602 hospital stays (+ 0,53 % compared with 2018)
18,472 consultations (- 1.5 % compared with 2018)
38 trials open, including 3 phase I-I/II trials

Strategic objectives: The breast cancer OCC has four strategic objectives: provide and update a "personalized after-cancer program" at the end of adjuvant treatment and adopt a multidisciplinary approach in order to provide more personalized care during the metastatic phase; expand clinical research by sponsoring more clinical trials and carrying out trials relating to every aspect of the Breast Cancer OCC's work; integrate metabolism-centered translational research (on the sterols–breast cancer-adipocytes theme) into clinical activities; optimize regional cooperation with respect to training and research.

• A regional referral center for breast cancer radiology

The IUCT-Oncopole's Imaging Department includes a specialist breast cancer radiology unit with a tomosynthesis machine (3D mammography), acquired in 2018. The unit was restructured in 2019 in order to optimize patient pathways.

• Regional knowledge-sharing collaborations

Discussions between the IUCT-Oncopole and cancer care facilities in Montpellier, undertaken following the formation of the Occitanie Region, led to several actions being taken in 2019:

• Creation of a mechanism to jointly examine possibilities for prospective clinical trials;
• Creation of an inter-university diploma in "Breast Cancer: From Physiology to After-Cancer";
• Organization of the first Occitane Breast Cancer Meeting, supported by the Onco-Occitanie network (the next edition is planned for March 2020);
• Publication of the first Breast Cancer–Occitanie Thesaurus, produced by updating the thesaurus for the former Midi-Pyrénées region.

• Pink October: a great success in 2019

For the fourth year in a row, as part of the Pink October breast cancer awareness month, the IUCT-Oncopole ran a "Life after Cancer" day, which included 16 relaxation and well-being workshops, presentations, and a forum for cancer associations. In addition, a special training evening, called "Je Dis Rose", attracted around 60 healthcare professionals from across the region. On a more artistic level, the IUCT-Oncopole's façade was lit up in pink every evening during the month.

• Research projects in collaboration with the CRCT

Research conducted in collaboration with CRCT team 12 (Dr M. Poirot & Dr S. Silvente-Poirot) established a link between a cholesterol derivative, dendrogenin A (DDA) and cancerous tumors. This finding is the basis for the EPOXCAN project, which was launched in 2019 to more precisely determine the role of the metabolic deregulation of DDA in breast cancer. Another project—to explore the tumor microenvironment in ER-positive, HER2-negative breast cancers—will soon be launched in collaboration with CRCT team 20 (Dr S. Valitutti).

• SAFIR 02 Immuno au San Antonio Breast Cancer Symposium 2019

Prof. F. Dalenc presented the results of the SAFIR 02 Immuno randomized phase-II trial at the 2019 San Antonio Breast Cancer Symposium. This study, conducted as part of the SAFIR02-breast project, coordinated by Prof. F. André (Institut Gustave Roussy) and Dr T. Bachelot (Léon Bérard Center), compared the efficacy of maintenance chemotherapy with that of durvalumab (PDL1 inhibitor) in non-progressive HER2-negative breast cancer patients after chemotherapy. In terms of overall survival, results supported the use of immunotherapy in patients with triple-negative breast cancer and/or breast cancer expressing PDL1.

Main collaborations: CRCT teams 1 (Prof. G. Favre), 2 (Dr M-J. Pillaire), 7 (Prof. P. Brousset), 12 (Dr M. Poirot & Dr S. Silvente-Poirot) and 20 (Dr S. Valitutti), and the CNRS-IPBS "Cancer Microenvironment and Adipocytes" team, UMR 5089 (Prof. C. Muller).

Selected publications in 2019 :

. D'Hondt, V. et al. **UCBG 2-04: Long-term results of the PACS 04 trial evaluating adjuvant epirubicin plus docetaxel in node-positive breast cancer and trastuzumab in the human epidermal growth factor receptor 2-positive subgroup**. *Eur. J. Cancer* **122**, 91–100 (2019).

. Pons-Tostivint, E. et al. **Survival Impact of Locoregional Treatment of the Primary Tumor in De Novo Metastatic Breast Cancers in a Large Multicentric Cohort Study: A Propensity Score-Matched Analysis.** Ann. Surg. Oncol. 26, 356–365 (2019).

. Puszkiel, A. et al. **Factors affecting tamoxifen metabolism in breast cancer patients; preliminary results of the French PHACS study (NCT01127295)**. Clin. Pharmacol. Ther. (2019) doi:10.1002/cpt.1404.

. Vaysse, C., et al. **France: The First Country to Ban a Type of Breast Implant Linked to Anaplastic Large Cell Lymphoma**. Aesthet Surg J (2019) doi:10.1093/asj/sjz142.

IUCT-O OCC
GYNECOLOGICAL CANCERS

Coordinator: Dr Laurence GLADIEFF

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**787 (- 0.88%)**
Surgery	**332 (- 4.87%)**
Chemotherapy	**353 (- 1.67%)**
Radiotherapy	**105 (- 7.08%)**
Brachytherapy	**177 (+ 11.32%)**

17 physicians
5,562 hospital stays (- 5.8 % compared with 2018)
3,697 consultations (+ 4.4 % compared with 2018)
17 trials open, including 2 phase I-I/II trials

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

Strategic objectives: The Gynecological cancers OCC focuses on four key themes: treatment for peritoneal carcinomatosis (from initial characterization to palliative care); complex surgery for pelvic relapses of gynecological cancer and reconstruction techniques; links between immunity and ovarian and cervical cancers; and 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" (TMRO) 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 addition, several of the OCC's physicians helped draft the Saint Paul de Vence Guidelines for Clinical Practice, which were unveiled in January 2019 at the 18th Francophone Conference on Breast and Gynecological Cancers.

• Numerous contributions to online training for healthcare professionals

During 2019 the OCC's physicians, in collaboration with the French Society for Oral Surgery, ran several webinars on Oncostream, the leading medical e-learning web TV station.

Since 2018 Drs. C. Martinez Gomez, M.A. Angeles, A. Martinez and G. Ferron have been writing a series of ten-step guides to different surgical techniques, each accompanied by a specially made video.

In 2017 the European Society of Gynaecological Oncology certified the IUCT-Oncopole as a gynecological oncology training center. Dr C. Martinez Gomez became the new training program's first graduate in 2019. Only seven other centers in France are accredited to provide these top-level courses.

• Research in collaboration with the CRCT

The OCC works closely with CRCT team 1 (Coordinator: Prof. M. Ayyoub/J-P. Delord) to investigate T cell responses to tumor antigens. Two clinical trials were launched in 2019 in order to constitute an "immune-bank" of samples from patients receiving immunotherapy (MINER trial) or other therapies (DECIdE trial). These samples will be used to study links between tumor antigens, the T cell anti-tumor response and lymphocyte inhibition mechanisms. Another study, conducted under the auspices of the GINECO and in collaboration with AstraZeneca, will assess an anti-HPV vaccination program with a single dose of anti-CTLA4 in patients with locally advanced cervical cancer.

During 2020 the OCC will also continue its collaboration with CRCT team 19 (coordinator: Dr F. Chibon) to identify the CINSARC genetic signature's potential for characterizing ovarian tumors. This study is part of the OvaSarc project, which received a GIRCI SOHO APIK grant in 2019.

Main collaborations: CRCT teams 1 (Prof. M. Ayyoub/J-P. Delord) and 19 (Dr F. Chibon)

Selected publications in 2019 :

. Angeles, M. A., Martínez-Gómez, C., Martinez, A. & Ferron, G. **En bloc pelvic resection for ovarian carcinomatosis: Hudson procedure in 10 steps**. Gynecologic Oncology 153, 209–210 (2019).

. Naour, A. L. et al. **Tumor cells educate mesenchymal stromal cells to release chemoprotective and immunomodulatory factors**. J Mol Cell Biol (2019)

. Voglimacci, M. et al. **Chemoradiotherapy for locally advanced cervix cancer without aortic lymph node involvement: can we consider metabolic parameters of pretherapeutic FDG-PET/CT for treatment tailoring?** Eur. J. Nucl. Med. Mol. Imaging (2019)

IUCT-O OCC
SARCOMAS

Coordinator: Dr Christine CHEVREAU

Indicators	Value (comparison with 2018)
MDT meetings	49 (0%)
Files	1,177(-0.42%)
Patients	678 (+ 1.18%)

16 physicians
338 new patients each year
18 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: The Sarcomas OCC continues to structure the provision of care for patients in the region with soft tissue and bone sarcomas. It is also extending its translational research activities by coordinating the national SARRA project and by working with the ONCOSARC team (CRCT team 19 – Dr F. Chibon) to optimize the CINSARC genomic signature.

• An national expertise center

The IUCT-Oncopole, via the Institut Claudius Regaud, has been designated a national expertise center within France's new NETSARC+ network. Validated by the INCa in 2019, NETSARC+ brings together the NETSARC clinical network, the RRePS pathology network and the RESOS bone tumor network.

• A structured approach to treating AYA patients

Care provision for AYA cancer patients (15 – 25 years old) at the IUCT-Oncopole is based on an established INCa approved model that was developed by the Sarcoma OCC. This model categorizes AYA patients into the following 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). In 2019 the AJAMIP team, in conjunction with the Onco-Occitanie network, created a procedure for providing non-medical care to these patients.

• Changes to radiation therapy

Preoperative radiotherapy is now the preferred treatment mode, as it provides identical local control, enables volumes to be determined more accurately and allows radiation doses to be reduced, thereby lowering long-term toxicity risks. Similarly, intensity modulation is used whenever possible, which means using optimal positioning systems and image-guided radiation therapy. A doctoral research project was launched in 2019 to study the value of adaptative radiotherapy in treating sarcomas (evaluation of target coverage as a function of tumor volume).

• Collaboration with the French Sarcoma Group (GSF)

Prof. A. Gomez-Brouchet is a member of the French Sarcoma Group's GROUPOS network, whose members are working towards homogenizing practices by creating standardized bone-tumor resection reports that take into account histopathological modifications to tumors following chemotherapy. The Sarcoma OCC, in collaboration with GROUPOS and the Bone Tumor Study Group (GSF-GETO/RESOS), is studying ways of evaluating the resection margins of bone sarcomas treated using neoadjuvant chemotherapy.

Main collaboration: Interconnexions with ONCOSARC team (CRCT 19 - Dr F. Chibon)

Selected publications in 2019 :

. Valentin, T., Lesluyes, T., Le Guellec, S., Chibon, F. **Chemotherapy in localized soft tissue sarcoma : will we soon treat grade 1 tumors ?** Ann. Oncol. 2019.

. Duazo-Cassin L, Le Guellec S, Lusque A, Chantalat E, Laé M, Terrier P, Coindre JM, Boulet B, Le Boulc'h M, Gangloff D, Meresse T, Chaput B, Al Ali A, Rimareix F, Bonvalot S, Vaysse C. **Breast desmoid tumor management in France : toward a new strategy. Breast Cancer Res Treat. (2019)**

. Sylvie Bonvalot et al. **NBTXR3, a First-In-Class Radioenhancer Hafnium Oxide Nanoparticle, Plus Radiotherapy Versus Radiotherapy Alone in Patients With Locally Advanced Soft-Tissue Sarcoma (Act.In.Sarc): A Multicentre, Phase 2-3, Randomised, Controlled Trial.** Lancet Oncol. 2019

. Maud Toulmonde et al. **Pazopanib or Methotrexate-Vinblastine Combination Chemotherapy in Adult Patients With Progressive Desmoid Tumours (DESMOPAZ): A Non-Comparative, Randomised, Open-Label, Multicentre, Phase 2 Study.** Lancet Oncol. (2019)

IUCT-O OCC
HEMATOLOGY

Coordinator: Prof. Christian RECHER

14 physicians
15,599 hospital stays (+ 12.26 % compared with 2018)
11,023 consultations (+ 2.7 % compared with 2018)
8 patients treated using CAR-T-cells
87 trials open, including 5 phase I/I-II

Activity	Active files, escluding oral therapies (change compared with 2018)
Total	1,688 (+ 10.11%)
Chemotherapy	1,179 (+ 18.02%)
Radiotherapy	131 (- 5.76%)

Type of transplant	N°hospital stays (change compared with 2018)
Transplants	187 (- 1.58%) comprising:
Allogenic transplants	72 (+ 10.77%)
Autologous transplants	115 (- 8%)

Strategic objectives: The Hematology OCC's work focuses on six main themes: expanding patient capacity; extending outpatient treatment; optimizing cooperation with its network (shared time); increasing early phase clinical research for intensive treatments (acute leukemia, CAR-T cells, HSC transplants) and evaluation (real-time molecular diagnoses, residual diseases, clonal selection); developing real-world clinical research (databases, medication, pharmacology, practices, molecular epidemiology); and integrating translational research into clinical practice (molecular, phenotype, 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 treating non-Hodgkin lymphomas (NHL). It is also a member of several French networks, including IFM, FILO, fi-LMC/GRAALL, FIM, SFGM-TC and LYSA.

• The first patients treated by CAR-T cells
CAR-T cells are T lymphocytes that are harvested from a patient and then genetically modified in vitro so they express an artificial ("chimeric") receptor capable of recognizing a tumor antigen. Close collaboration between the Hematology OCC, the Intensive and Continuing Care Department, the Pharmacy, the French Blood Service and the Onco-Occitanie network enabled its OCC to obtain its first two Gilead and Novartis accreditations in 2019. The first patient was treated in July 2019.

• JACIE accreditation
2019 saw the OCC take the final steps towards obtaining the IUCT-Oncopole's first JACIE (Joint Accreditation Committee of ISCT-Europe and EBMT) accreditation. Adapted from the American FACT program, JACIE is a European accreditation program that promotes high quality standards and good practices in every aspect of hematopoietic stem-cell transplants and cell therapy. Certification was awarded in January 2020, following successful audits of the IUCT-Oncopole's transplant service and operating suite, and the French Blood Service's cytapheresis unit.

• Hematology TPE
Two new therapeutic patient education (TPE) programs were launched in 2019 to help patients receiving hematopoietic stem-cell transplants. The project, coordinated by Dr A. Huynh, comprises a pre-transplant program ("3, 2, 1... Prêt? Greffe!" – contact person: L. Mercier) and a post-transplant program ("Le MAG (MonAlloGreffe): A La Une !" – contact person: F. Carantois), both of which are aimed at patients over the age of 15. Their goal is to reduce anxiety and prevent complications by informing patients about the transplant process, helping them prepare for it, both physically and mentally, and teaching them the necessary self-care skills.

•A framework agreement to develop personalized medicine
A framework agreement signed with ROCHE in 2019 will enable the IUCT-Oncopole and ImCORE to launch the "THALYES 2020-22" project. Sponsored by Prof. L. Ysebaert and based on a collaboration with CRCT team 9 (coordinator: Prof. C. Laurent), THALYES 2020-22 will use biopsies from patients with lymphomas to draw up 3D models of tumors that can be used to test drugs. The aim is to be able to offer patients truly personalized treatments in the very near future.

• Optimizing coordination of hematology clinical trials
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 Clinical Trials Office with respect to phase I trials relating to acute leukemia.

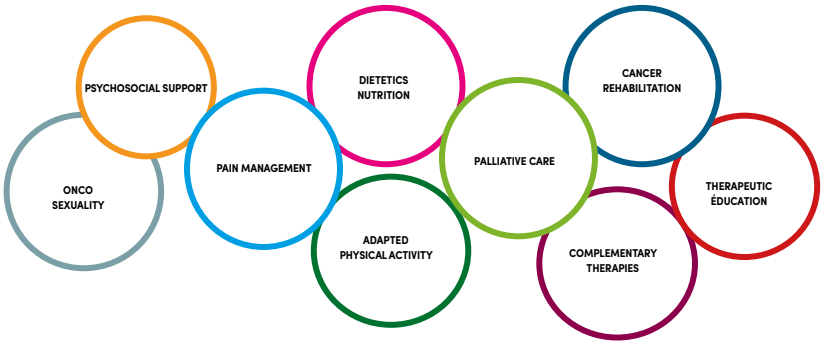
Main collaborations: CRCT teams 9 (Dr J-J. Fournié), 13 (Prof. H. Avet-Loiseau & Dr L. Martinet), 16 (Prof. E. Delabesse) and 18 (Dr J-E. Sarry)

Selected publications in 2019 :

.Attal, M. *et al.* **Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study**. *Lancet* (2019)
. Perl, A. E. et al. **Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML.** N. Engl. J. Med. 381, 1728–1740 (2019)
. Perrot, A. et al. **Development and Validation of a Cytogenetic Prognostic Index Predicting Survival in Multiple Myeloma**. J. Clin. Oncol. JCO1800776 (2019)
. Series, J. et al. **Differences and similarities in ibrutinib and acalabrutinib effects on platelet functions**. Haematologica (2019)
. Ysebaert, L. et al. **Oncology nurse phone calls halve the risk of reduced dose intensity of immunochemotherapy: results of the randomized FORTIS study in chronic lymphocytic leukemia**. Ann. Hematol. 98, 931–939 (2019).

IUCT-O OCC
SUPPORTIVE CARE (DISSPO)

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



10 physicians and 12 outside practitioners
Almost 10,000 supportive care opinions and consultations
More than 35,000 procedures carried out by supportive care professionals
5,420 new patients benefitted from at least one supportive care intervention in 2019
More than 750 hours of courses/ training provided

Strategic objectives: The Supportive Care OCC focuses on four main themes: incorporating rehabilitation into care pathways at an early stage; integrating therapeutic patient education into outpatient pathways and expanding the Oral Anticancer Drugs program in the region; extending the use of intrathecal analgesia across the region; and conducting research projects in every area of supportive care.

• Regional referral center for therapeutic education:
At the request of Occitanie Regional Health Agency, the IUCT-Oncopole coordinates a Transversal Therapeutic Patient Education Unit for cancer patients in the region. The unit's main roles are to expand TPE for cancer patients in Occitanie and to continue setting up a TPE center for patients receiving oral chemotherapy.

• Novel initiatives and partnerships
. A convention has been signed with Toulouse Institute of Osteopathy to provide consultations, every Friday, to patients in the hospitalization departments.
. The regional branch of the ONCODIETS network, France's leading network of independent cancer nutritionists, was formally launched during a training day in December 2019.
. In response to the increasing complexity of social care for patients, the Supportive Care OCC, in partnership with CARSAT (regional retirement and healthcare fund), has begun organizing quarterly meetings to inform patients about their social security rights. The first meeting took place in June 2019.

• Sport & Cancer Center
The IUCT-Oncopole's Sport & Cancer Center enables cancer patients to take part, free of charge, in adapted physical activity sessions. Created in 2017, it is one of 25 such centers funded by CAMI Sport & Cancer and its partners across France. Stade Toulousain Rugby Club joined the program in 2018 and offers patients sports therapy sessions at its Ernest-Wallon Stadium. In October 2019 the club joined forces with the Les Rubies rugby and cancer association and Malakoff Médéric Humanis to run a "Sport & Cancer Day" for the public and healthcare professionals.

• Focus on cancer rehabilitation
The Supportive Care OCC is working on integrating rehabilitation into cancer care pathways at a much earlier stage by introducing pre-rehabilitation into three pathways: sarcomas, major pelvic surgery and hematology (blood transplants).

• New research projects in 2019
Three new projects obtained funding in 2019: Efficacy of Pre-Operative Rehabilitation in Patients with Limb Sarcomas (EPOP, Ligue Contre le Cancer); TEC-ORL, a phase II randomized comparative trial to evaluate the use of Qutenza when treating patients in remission from head and neck cancers experiencing chronic neuropathic pain (PHRCI - GIRCI SOHO); and "Le off: l'autre séance" - evaluation and feedback, proposition and validation of innovative practices in care pathways for AYA patients (Fondation de France). This final study evaluates the need to explain medical treatment during hospitalization (Cure), taking into account the specific psychosocial needs (Care) of adolescent and young adult patients (15-25 years old) with hematological cancers.

Main collaboration: IFERISS-CRESCO team (Prof. T. Lang)

Selected publication in 2019 :
. Molin, Y. et al. **PALLIA-10, a screening tool to identify patients needing palliative care referral in comprehensive cancer centers: A prospective multicentric study (PREPA-10)**. Cancer Med (2019)

IUCT-O OCC
HEAD AND NECK CANCERS

Coordinators: Prof. Sébastien VERGEZ and Dr Michel RIVES

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**740 (+ 0.14%)**
Surgery	**179 (- 9.6%)**
Chemotherapy	**298 (+ 5.3%)**
Radiotherapy	**301 (- 6.81%)**
Brachythérapy	**12 (+ 50%)**

15 physicians
10,482 hospital stays (- 13.05 % compared with 2018)
7,417 consultations (+ 0.67 %)
26 trials open, including 3 phase I-I/II trials

Strategic objectives: The Head and Neck OCC's objectives are to optimize care pathways and to develop knowledge-sharing activities. It is also extending its research activities by sponsoring and conducting more clinical trials in every area of its activities.

• 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 anatomopathology and in sinus, cranial base and salivary gland surgery.

• Production of regional and national guidelines
In 2019 the OCC, in collaboration with the Onco-Occitanie network, Toulouse University Hospital-Larrey, Toulouse University Hospital-Purpan, and the Clinique Pasteur, updated the regional care guidelines for head and neck cancers. A regional review is in progress. 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). All of these guidelines will be published in 2020.

• Innovative surgical reconstructions
The plastic surgery and head & neck surgery teams enjoy a close, long-standing and highly fruitful collaboration that allows them to perform increasingly complex and ambitious surgical reconstructions. Joint studies between the two teams have resulted in two papers on cervical-facial reconstruction, most notably involving the super-thin external pudendal artery (STEPA) free flap, a new flap studied by Dr A. Dupret-Bories*.

• First trial for patients with cancer of viral origin
CITHARE is a randomized, phase II clinical trial for patients with cancer of the upper aerodigestive tract linked to the HPV virus. Its aim is to enable these patients to be treated by immunotherapy and to identify the role of immune escape in the disease's progression from its origin in a lymph organ. This is the first prospective randomized trial specifically for patients with a virus-associated cancer of the oropharynx. Sponsored by the IUCT-Oncopole and coordinated by Dr A. Modesto, CITHARE is funded by AstraZeneca and involves another French center (Clermont-Ferrand). Inclusions will continue until the end of 2020. An ancillary immuno-monitoring study is being conducted in collaboration with CRCT team 1 (Prof. M. Ayyoub/J-P. Delord).

• Knowledge sharing
Since 2017, and after focusing on optimizing care pathways, the Head and Neck cancers OCC has begun developing its knowledge-sharing activities by organizing post-university teaching courses and scientific events for professionals at the IUCT-Oncopole and throughout the region.

Main collaborations: CRCT team 1 (Prof. M. Ayyoub/J-P. Delord) and the CIRIMAT research group - UMR CNRS INPT UPS 5085 (Prof. C. Laurent)

Selected publications in 2019 :

. *Dupret-Bories, A. et al. **The super thin external pudendal artery (STEPA) free flap for oropharyngeal reconstruction - A case report.** Microsurgery (2019)
. Le Louedec, F. et al. **Cetuximab Pharmacokinetic/Pharmacodynamics relationships in advanced head and neck carcinoma patients**. Br J Clin Pharmacol (2019)
. Modesto, A. et al. **Definitive radiochemotherapy or initial surgery for oropharyngeal cancer : To what extent can p16 expression be used in the decision process?** Strahlenther Onkol (2019)
. Potet, P. et al. **Closure of radial forearm free flap donor site: A comparative study between keystone flap and skin graft**. Head Neck (2019)

IUCT-O OCC
NEURO-ONCOLOGY

Coordinators: Prof. Elizabeth MOYAL and Dr Delphine LARRIEU-CIRRON

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**324 (+ 8.72 %)**
Chemotherapy	**166 (+ 2.47 %)**
Radiotherapy	**175 (+ 5.42 %)**

5 physicians
5,691 hospital stays (+ 13.39 %)
1,176 consultations (+ 18.2 %)
4 trials open, including 2 phase I-I/II trials

Strategic objectives: The OCC has carried out translational research for many years, focusing on two main themes: "radiotherapy and targeted therapies", and "metabolic imaging for predicting responses to radiotherapy and for monitoring radiotherapy-chemotherapy combinations".

• International recognition
The numerous innovative clinical trials sponsored and/or conducted by the IUCT-Oncopole, especially phase I trials of targeted therapies, have resulted in the institute becoming an international referral center for neurological cancers. The OCC is also a regional case review center for reirradiation following immunotherapy.
Prof. E. Moyal was invited by Dr M. Valiente, of the Spanish National Cancer Research Center in Madrid, to co-sponsor the "S100A9-dependent radiation resistance in brain metastasis" study. As part of this project, which is funded by Worldwide Cancer Research, Prof. Moyal is supervising a medical PhD thesis whose results should be published in 2020.

• Member of leading networks
Prof. Moyal is a member of the European Association of Neuro-Oncology's Scientific Committee and helped draw up the program for the Society's 2019 congress in Lyon. Furthermore, Prof. Moyal and Dr D. Larrieu-Cirron have both been members of the board of the Association of Francophone Neuro-Oncologists (ANOCEF) since 2018.

• Contribution to CAR-T cell therapy
Since August 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, most notably to take into account the new therapy's side effects. Hence, Dr D. Larrieu-Ciron has been tasked with coordinating responses to the complications and neurological toxicities associated with CAR-T cells.

• Research within France's POLA network
Analyses of cohorts from France's POLA network (affymetrix and clinical data – coordinators at Toulouse: Prof. E. Uro-Coste and Prof. E. Moyal) enabled Prof. Moyal and J. Gilhodes to identify a multi-gene signature that can be used to predict the radiosensitivity of patients with high-grade oligodendrogliomas. These results were presented at ASCO 2019. Moreover, POLA also includes a doctoral study to compare radiotherapy + temozolomide chemotherapy with radiotherapy + PCV chemotherapy for patients with IDH-mutant astrocytoma. Results of this study, which was supervised by Prof. Moyal, support the use of radiotherapy + PCV chemotherapy. A paper presenting these results has been submitted.

• Grants awarded under the ARC's first SIGN'IT competitive grant scheme
The SI2GMA (Stereotactic Irradiation and Immunotherapy Glioblastoma Markers) project, which was awarded funding under the ARC's first SIGN'IT competitive grant scheme, builds on data obtained during the STERIMGLI phase I-II trial (study of combined hypo-fractionated stereotactic radiation therapy and the anti-PDL1 durvalumab in patients with recurrent glioblastoma). Launched in April 2019 and coordinated by Prof. Moyal, SI2GMA is the fruit of a collaboration between the Radiotherapy and Medical Physics Departments, the Oncogenetics Laboratory, the Pathology Department, CRCT teams 1 (Prof. M. Ayyoub/J-P. Delord) and 11 (Prof. E. Moyal & Dr C. Toulas), and Grenoble Institute of Neurosciences.

• SILK: a project to treat brain metastases
2019 also saw the launch of the SILK project, a multi-center, phase II randomized study coordinated by Prof. Moyal and Dr J. Khalifa. SILK's objective is to compare the efficacy of stereotactic radiosurgery with and without immunotherapy in lung cancer patients with brain metastases.

Main collaborations: CRCT team 11 (Prof. E. Moyal & Dr C. Toulas) and Inserm's ToNIC unit (Dr P. Péran)

Selected publications in 2019 :

. De Barros, A. et al. **Impact on survival of early tumor growth between surgery and radiotherapy in patients with de novo glioblastoma**. J. Neurooncol. (2019) doi:10.1007/s11060-019-03120-3.
. Deshors, P. et al. **Ionizing radiation induces endothelial transdifferentiation of glioblastoma stem-like cells through the Tie2 signaling pathway**. Cell Death Dis 10, 816 (2019).
. Kowalski-Chauvel, A. et al. **Alpha6-Integrin Regulates FGFR1 Expression through the ZEB1/YAP1 Transcription Complex in Glioblastoma Stem Cells Resulting in Enhanced Proliferation and Stemness**. Cancers (Basel) 11, (2019).
. Malric, L. et al. **Inhibiting Integrin β8 to Differentiate and Radiosensitize Glioblastoma-Initiating** Cells. Mol. Cancer Res. 17, 384–397 (2019).
. Siegfried, A. et al. **EWSR1-PATZ1 gene fusion may define a new glioneuronal tumor entity.** Brain Pathol. 2019 Jan;29(1):53-62

IUCT-O OCC
ONCOGENETICS

Coordinator: Prof. Rosine GUIMBAUD

N°of consultations	
1st consultation for a relative:	493
1st consultation for an index case:	656
Support and/or communication of results:	887

7 physicians
2,355 consultations in 2019
190 cases presented in MDT meetings, including 136 for breast/ovarian syndromes and 54 for digestive syndromes
3 clinical trials specifically devoted to oncogenetics

Strategic objectives: The Oncogenetics OCC's main goal is to respond to changing needs in the region's demand for genetic testing, while improving overall care for individuals with a hereditary predisposition to cancer. Measures to achieve this include providing psychological support to individuals undergoing genetic testing and creating regional multidisciplinary review teams. Finally, to meet the need for new molecules for targeted therapies, it is planned to widen indications for therapies that depend on a patient's genetic profile (e.g., PARP).

• Regional coordination to optimize support for patients

The Oncogenetics OCC coordinates the Occitanie-Ouest region's three genetic testing centers (IUCT-Oncopole, Clinique de l'Ormeau and Rodez Hospital). It also organizes weekly regional MDT meetings and, in 2019, set up a regional polyposis MDT of specialists from centers across the region, who meet by videoconference. The OCC also works closely with the IUCT-Purpan (Toulouse), the Clinique Pasteur (Toulouse) and the Onco-Occitanie regional cancer network in order to provide monitoring programs for breast-ovarian cancer syndrome, Lynch syndrome and familial adenomatous polyposis.

Also in 2019, the OCC began providing consultations for neuroendocrine cancers, with the appointment of an extra physician (Dr S. Grunenwald). These consultations are carried out in conjunction with the IUCT-Rangueil/Larrey's Endocrinology, Metabolic Diseases and Nutrition Department.

• Founder member and coordinator of the GENEPY network

GENEPY is the name of the regional oncogenetics network the IUCT-Oncopole, Clinique Pasteur and Onco-Occitanie regional cancer network set up to improve support for individuals with a hereditary predisposition to breast and ovarian cancers, colorectal and endometrial cancers and, as of 2019, Lynch syndrome. Coordinated by the Oncogenetics OCC, GENEPY brings together oncogenetics consultants and other healthcare professionals in public institutions, private establishments or private practice (298 members in total) to ensure patients receive optimal care, in line with INCa recommendations. In 2019 Drs. L. Gladieff and B. Boulet took over responsibility for coordinating breast and ovarian cancer syndrome, and a new committee was appointed to improve the way the unit is organized, optimize monitoring of women with a predisposition for this type of cancer, and create and update guidelines and awareness raising materials.

• A novel initiative to discuss predispositions to cancer

"BRCA Café" is a discussion group for women with a hereditary predisposition to breast and ovarian cancer (carriers of BRCA-1, BRCA-2 and PALB2 genetic mutations) that meets every two months at "Les Fortes Têtes", a relaxed and friendly restaurant in the center of Toulouse. This novel initiative was launched in September 2018 by J. Grondin (OCC Oncogenetics) under the auspices of the GENEPY network. Twenty-one women attended BRCA Café meetings (max. 10 people per session) during the project's first year, with discussions mostly centering round understanding the results of genetic tests, prophylactic surgery and explaining genetic information to family and friends.

Main collaboration: CRCT team 2 (Dr M-J. Pillaire)

Selected publications in 2019 :

. Girard, E. et al. **Familial breast cancer and DNA repair genes: Insights into known and novel susceptibility genes from the GENESIS study, and implications for multigene panel testing**. Int. J. Cancer 144, 1962–1974 (2019).
. Surun, A. et al. **Medulloblastomas associated with APC germline pathogenic variant share the good prognosis of CTNNB1 mutated medulloblastomas**. Neuro-oncology (2019)
. Vande Perre, P. et al. **Germline mutation p.N363K in POLE is associated with an increased risk of colorectal cancer and giant cell glioblastoma.** Fam. Cancer 18, 173–178 (2019).

IUCT-O OCC
SKIN CANCERS

Coordinators: Prof. Nicolas MEYER and Dr Dimitri GANGLOFF

Activity	Active files, excluding oral therapies (charge compared with 2018)
Total	**694 (+ 4.36%)** including 451 for melanomas (+ 3.44 %)
Surgery	**368 (+ 3.08%)** including 239 for melanomas (+ 4.37 %)
Chemotherapy	**281 (+ 20.6%)** including 228 for melanomas (+ 20 %)
Radiotherapy	**119 (+ 1.71%)** including 59 for melanomas (+ 5.36 %)
Brachytherapy	**4 (-33.33%)**

21 specialists
4,226 hospital stays (+ 0.02 %) including 2,183 for melanomas (+ 2 %)
6,695 consultations (- 1.5 %) including 2,140 for melanomas (+ 1.5 %)
17 clinical trials ongoing, including 4 phase I-I/II trials

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, the OCC helped draw up the guidelines published by the European Society for Medical Oncology in 2019, notably by characterizing toxicities associated with immunotherapies. 2019 also saw the creation of the European Network for Cutaneous Adverse Events to Oncologic Drugs (ENCADO) at the initiative of Dr V. Sibaud and in collaboration with Federico II University Hospital, in Naples, and Fuenlabrada University Hospital, in Madrid. ENCADO is Europe's first network specializing in the dermatological toxicities of cancer treatments.

• New 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, in the light of recently published research, curettage of micrometastases is no longer carried out systematically but based on personalized indications and as a function of the adjuvant treatment being followed by each patient. Finally, a doctoral research project examining the oncological safety of perforator flap reconstructive surgery will begin in 2020. This innovative technique takes into account the anatomy and function of the areas in question and could replace the current technique of direct excision of the structure.

• Improving hospital-city links

With the arrival of adjuvants in immunotherapy and their associated side effects, a team of coordinating nurses has been set up to monitor patients at home, so they can leave hospital as soon as possible after treatment. For some patients, it may even be possible to avoid some hospital stays. The team will monitor healing in conjunction with community nurses and, in the case of oral chemotherapy, with the patient's entire healthcare network. Several treatments, including immunotherapy are now administered by home care units. In addition, Dr V. Pelagatti and Dr C. Vinson have set up an oral therapy drug-dose adaptation mechanism that includes the patient and the patient's pharmacist and family doctor.

• Completion of stage 1 of TICIMEL

The OCC coordinates and contributes to several clinical trials. 2019 saw the completion of the first stage of the TICIMEL phase 1b trial to evaluate the safety of administering nivolumab and ipilimumab in combination with certolizumab or infliximab in patients with advanced melanomas. Initial results will be published in 2020.

Main collaborations:CRCT teams 3 (Prof. G. Favre) and 4 (Prof. T. Levade & Dr N. Andrieu)

Selected publications in 2019 :

. Bilal, F. et al. **Sphingomyelin Synthase 1 (SMS1) Downregulation Is Associated With Sphingolipid Reprogramming and a Worse Prognosis in Melanoma**. Front Pharmacol 10, 443 (2019).

. Chabrillac, E. et al. **Cutaneous Squamous Cell Carcinoma Tumour Size is Associated with Sentinel Lymph Node Metastasis in a Cohort of 69 Patients.** Acta Derm. Venereol. (2019) doi:10.2340/00015555-3293.

. Deilhes, F., Boulinguez, S., Pagès, C., Paul, C. & Meyer, N. **Advanced Cutaneous Squamous Cell Carcinoma Is Associated with Suboptimal Initial Management in a Cohort of 109 Patients**. Dermatology (Basel) 1–6 (2019).

. Sibaud, V. et al. **Nivolumab-related mucous membrane pemphigoid**. Eur. J. Cancer 121, 172–176 (2019).

IUCT-O OCC
GERIATRIC ONCOLOGY

Coordinators: Dr Loïc MOUREY and Dr Laurent BALARDY

Geriatric evaluations by	N° evaluations
Mobile Geriatric Oncology Team (EMOG)	1,437
Registered nurse on IUCT-O site	147

6 specialists

Strategic objectives: The Geriatric Oncology OCC meets the needs of older patients at all three IUCT sites by ensuring they have access to the most appropriate care and most innovative therapies, wherever they first receive treatment. The OCC's current projects include working with the regional cancer network to roll out a Shared Medical Record System (Dossier Communicant de Cancérologie) that will improve patient monitoring and follow-up care by facilitating communication between the hospital and family doctors. It is also sponsoring research projects aimed at meeting future challenges in geriatric oncology.

• A key component in the Geriatric Oncology Coordination Unit

The Geriatric Oncology OCC, Toulouse University Hospital's Geriatrics Department and the Onco-Occitanie regional cancer network work together closely within the Midi-Pyrénées Geriatric Oncology Coordination Unit. Medical coordination is provided by a geriatrician and an oncologist, supported by an assistant attached to the regional cancer network. A Mobile Geriatric Oncology Team has also been created to provide specialist expertise to the IUCT's departments and other hospitals in the region. Occitanie's two Geriatric Oncology Coordination Units came together in 2019 to define a joint road map.

• Development of a Chatbot app to improve monitoring of older patients

Telephone monitoring by specially trained nurses can identify side effects or non-compliance with treatment. In 2019 following a local call for proposals, the Geriatric Oncology OCC introduced a smartphone app in which a chatbot analyzes patients' answers to standardized questions in order to avoid unnecessary telephone calls. This app has been patented, as allowed for under Article 51 of France's Social Security Financing Act of 2018.

• Creation of a geriatric oncology 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. The first session will open on March 6, 2020. The Geriatric Oncology OCC also helps teach the University Diploma in Geriatric Oncology, which was awarded to 14 students in 2018-2019.

• Regional targeted information campaigns

Two communication campaigns were carried out in 2019, one aimed at healthcare professionals, the other for the public. To this end, the Occitanie Geriatric Oncology Coordination Unit drew up an information leaflet for the region's doctors, in which it presented its objectives. It also helped distribute a French Geriatric Oncology Society (SOFOG) poster to independent nurses, pharmacists and family doctors. This work was mostly financed by the Occitanie Regional Health Agency.

• 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's Methodology Department, it has also developed a free statistical tool (R package) specially for clinical trials involving older patients. The forthcoming arrival of the INSPIRE project, sponsored by Prof. B. Velas at the Santé du Futur Campus, should strengthen research links on the theme of "aging and cancer".

Selected publications in 2019 :

. Bréchemier, D. et al. **Use of comprehensive geriatric assessment (CGA) to define frailty in geriatric oncology: Searching for the best threshold. Cross-sectional study of 418 old patients with cancer evaluated in the geriatric frailty clinic (G.F.C.) of Toulouse (France)**. J Geriatr Oncol (2019)

. Piau, A., Crissey, R., Brechemier, D., Balardy, L. & Nourhashemi, F. **A smartphone Chatbot application to optimize monitoring of older patients with cancer.** Int J Med Inform 128, 18–23 (2019).

. Steinmeyer, Z. et al. **Low lean mass and chemotherapy toxicity risk in the elderly: the Fraction study protocol**. BMC Cancer 19, 1153 (2019).

IUCT-O OCC
THYROÏD AND NEUROENDOCRINE CANCERS

Coordinators: Prof. Frédéric COURBON - Prof. Rosine GUIMBAUD - Prof. Delphine VEZZOSI

Activity	Active files, excluding oral therapies (charge compared with 2018)
Total	335 (- 3.18%)
Surgery	41 (+ 41.38%)
Chemotherapy	6 (+ 20%)
Radiotherapy	22 (+ 55.36%)
Radioactive iodine	256 (+ 8.02%)

22 specialists
867 hospital stays (+ 13.19 % compared with 2018)
1,077 consultations (+ 0.56 % compared with 2018)
7 clinical trials ongoing, including 1 prospective study

Strategic objectives: The OCC is a collaborative body involving departments from a number of establishments. It was created in 2018.

• A specific local structure

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.

Neuroendocrine tumors are treated by several departments at the IUCT-Rangueil/Larrey (PHU-MAD:[1] digestive oncology, gastroenterology, digestive surgery, internal medicine, radiology, pneumology and endocrinology) and the IUCT-Oncopole's Nuclear Medicine Department.

The OCC also includes two members of the IUCT-Oncopole's Pathology Department: Dr M. Danjoux, an expert in neuroendocrine tumors (national TEN-Path network), and Dr I. Rouquette, an expert in thyroid diseases.

Prof. F. Savagner (Biology Center, Purpan site), a member of the national TENGEN network, advises the OCC on endocrine tumor molecular biology.

• Nationally and internationally recognized expertise

Through its members, the IUCT-Oncopole is part of the National Study Group for Endocrine Tumors (GTE) and three INCa referral networks: RENATEN (neuroendocrine tumors), THUTHYREF (thyroid cancers) and COMETE (cancers of the adrenal capsule). The OCC also helped plan a national meeting in the field, being organized by INCa for January 2020. In addition, Dr S. Zerdoud is a member of the European Association of Nuclear Medicine's Thyroid Committee.

• A new European label in 2019

In 2019 the European Neuroendocrine Tumor Society certified the IUCT-Oncopole (Institut Claudius Regaud and Toulouse University Hospital) and IUCT-Rangueil/Larrey (Toulouse University Hospital) as a "European Centre of Excellence for Neuroendocrine Tumors". This certification, awarded following an application process steered by Prof. R. Guimbaud and Dr L. Dierickx, recognizes the IUCT's multidisciplinary expertise in recruitment, diagnosis and innovative treatments for rare neuroendocrine tumors, as well as its involvement in clinical research and in informing doctors about these pathologies. The newly accredited body, baptized "Toulouse University Centre Of Excellence for Neuroendocrine Tumors", is one of only four French centers (alongside Paris, Lyon and Marseille) to have obtained this certification.

• Specialist MDTs

The OCC has set up several MDTs: a neuroendocrine tumors MDT (RENATEN review MDT, Prof. R. Guimbaud), a neuroendocrine tumor molecular biology MDT, and three thyroid MDTs (Dr S. Zerdoud). The RENATEN MDT meets every two weeks and the neuroendocrine tumor molecular biology MDT meets every two months. The standard thyroid MDT meets every week, while the two specialist thyroid MDTs meet every two weeks (national TUTHYREF MDT – coordinator Prof. D. Vezzosi) or once a month (regional metastatic tumors review MDT).

• Ongoing research projects

Several research projects, conducted in collaboration with CRCT teams 12 (Dr M. Poirot & Dr S. Silvente-Poirot) and 14 (Prof. E. Chatelut), are ongoing. A highlight of 2019 was the launch of a new collaboration between Drs S. Zerdoud and L. Ménard within the "Optimization of the individualized patient dosimetry in radioactive iodine treatment of thyroid diseases" project, which is coordinated by Dr Ménard and funded by ITMO Cancer.

Main collaborations: CRCT teams 12 (Dr M. Poirot & Dr S. Silvente-Poirot) and 14 (Prof. E. Chatelut)

Selected publications in 2019 :

. Hindié et al. **Association of Radioactive Iodine Treatment of Hyperthyroidism with Cancer Mortality: an Unjustified Warning?** J Clin Endocrinol Metab. 2019

. Vija Racaru et al. **Diagnostic and Therapeutic Uptake of Intrathyroid Metastasis of Midgut Neuroendocrine Tumor on 68Ga-DOTANOC PET/CT and 177Lu-DOTATATE Imaging.** Clin Nucl Med. 2019

. Walter et al. **Everolimus after hepatic arterial embolisation therapy of metastases from gastrointestinal neuroendocrine tumours: The FFCD 1104-EVACEL-GTE phase II study**. Eur J Cancer. 2019

1. PHU-MAD = University-Hospital Center for Diseases of the Digestive System (located at Rangueil University Hospital).

IUCT-O OCC
UROLOGIC CANCERS

Coordinators: Prof. Bernard MALAVAUD, Dr Loïc MOUREY and Dr Pierre GRAFF-CAILLEAUD

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**945 (+ 6.42%)**
Chemotherapy	**312 (+ 1.3%)**
Radiotherapy	**351 (+ 5.09%)**
Brachytherapy	**82 (+ 28.13%)**

17 physicians
4,427 consultations (+ 1.8% compared with 2018)
38 trials open, inclunding 4 phase I-I/II trials

Strategic objectives: The Urologic Cancers OCC has several objectives: adopt a multidisciplinary approach (innovation, therapy, clinical research), propose and develop conservative treatments (bladder, prostate), and provide expertise on specific sectors of the population (adolescents and young adults; older adults).

• INCa-accredited referral center
The IUCT-Oncopole is an INCa-accredited referral center for prostate brachytherapy, an alternative technique to surgery for prostate cancers. For patients with more advanced tumors, brachytherapy is combined with external radiation therapy to increase the chances of success.

• Internationally recognized expertise
The Urologic Cancers OCC is a world pioneer in en-bloc endoscopic resection of bladder tumors, for which it has state-of-the-art instruments – notably high-definition endoscope cameras – thanks to a partnership with Olympus. Regular training sessions held by the OCC attract surgeons from throughout Europe. In addition, the OCC treats patients from across France, as it is one of only a few teams in the country to perform 3rd-generation remedial cryotherapy.

• Innovation at the heart of care
In order to define the best treatment options for localized prostate cancer, most patients receive targeted transrectal or transperineal biopsies, guided by multiparameter MRI (KOELIS system).
Moreover, all of our patients receive intensity-modulated radiation therapy (RapidArc or tomotherapy), using integrated imaging to reposition the beam for each treatment, and intraprostatic fiducial markers to ensure maximum precision. In the case of oligometastatic diseases, stereotactic radiotherapy is used for both intra-cerebral and extra-cerebral (bones, liver, lungs) locations.

• Collaborations with industry to promote innovation
In addition to its scientific and technical partnership with Olympus, the Urologic Cancers OCC has signed a framework contract with the Grenoble company KOELIS to provide an innovative image fusion system that is currently the subject of two doctoral theses, one in medicine and one in the sciences.
2019 saw the launch of ANTICIPATES, a trial (sponsored by CEPHEID) to determine whether biomolecular analysis of four specific genes can provide a reliable diagnostic test for cancer of the bladder. The objective is to replace bladder endoscopy (cystoscopy) by a simple urine test.
Finally, a collaboration with the German company MAVIG has been launched to study its recently developed "VivaScope", which allows confocal microscopy to be carried out in vivo. If results are conclusive, the aim is to use this tool to speed up prostate cancer diagnosis.

• A project awarded an INCa PHRC-K grant
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 trial, which was sponsored by Dr J. Khalifa, officially began in 2019, after receiving funding from the 2018 PHRC-K grant scheme.

Main collaborations: CRCT team 1 (Prof. M. Ayyoub / J-P. Delord) and the "Sphingolipids and Cancers" team at the Institute of Pharmacology and Structural Biology (CNRS – IPBS, Dr O. Cullivier).

Selected publications in 2019 :

. Covin, B. et al. **Refining the risk-stratification of transrectal biopsy-detected prostate cancer by elastic fusion registration transperineal biopsies**. World J Urol 37, 269–275 (2019)
. Ploussard, G. et al. **Added value of concomitant systematic biopsies for grade group prediction based on radical prostatectomy final pathology in MRI-positive patients undergoing fusion targeted biopsies**. J. Urol. 101097JU0000000000000418 (2019)

DEPARTMENT OF INTERNAL MEDICINE

Coordinator: Prof. Odile BEYNE-RAUZY

6 physicians
4,597 hospital stays (+4.9% compared with 2018), 82.3% of which were day-hospital stays
952 patients (+6.7% compared with 2018)
2,222 consultations (+1.6% compared with 2018)
2,086 LBP transfusion sessions (+23.3% compared with 2018)
658 non-scheduled acute cases treated (+42.4% compared with 2018), that is, 14.3% of cases
14 clinical trials open, including 1 phase I/I-II trial

Strategic objectives: The Department of Internal Medicine has a threefold remit: treat internal diseases, develop specific transversal activities, and include patients in trials investigating myelodysplastic syndromes, autoimmune cytopenia and hemoglobin diseases.

• Referral center for several conditions

The Department of Internal Medicine, led by Prof. O. Beyne-Rauzy, is one of four national referral centers for autoimmune cytopenia in adults (CeReCAI). It is also a center of expertise for "sickle cell disease and other rare red-blood-cell syndromes", for "thalassemia major and intermedia, other rare red-blood-cell syndromes and erythropoiesis", and for histiocytosis. Joint research into the child-adult transition and a joint therapeutic education program relating to these pathologies have been set up with the corresponding pediatric services.

• 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. Comon);
- Manage complex pathways (D. Yerle).

• Two themes for the anti-infections mission

2019 saw the creation of an MDT to treat invasive fungal infections. The new team holds two MDT meetings every month and works in collaboration with the IUCT-Oncopole's Hematology and Intensive/Continuing Care teams and the infectious diseases and microbiology departments at Toulouse University Hospital.
Vaccination for patients, their families and healthcare staff was another major focus for 2019. In order to increase the uptake of vaccinations, the department sent official guidelines on vaccines to family practitioners, gave patients information about vaccinations during consultations at the IUCT-Oncopole, and held meetings within all the IUCT-O's departments to raise awareness about vaccinations and offer healthcare staff vaccinations either within their department or from the occupational health service.

• Award of the "Hospitality" label

Following an audit by Toulouse University Hospital's quality, safety and user relations department, the Department of Internal Medicine was awarded the "Hospitality" label in October 2019. This label recognizes the attention given to quality, notably in terms of patient care, the information patients are given, the cleanliness and comfort of surroundings, and the cultural, relaxation and well-being services the department provides.

• Established expertise in myelodysplasia

The IUCT-Oncopole held a regional open day for patients with myelodysplastic syndromes as part of a national event designed to improve understanding of the disease, explain different treatments and their tolerances, and present the latest research findings. Feedback from the 70 patients and family members who attended the event was very positive.
In 2019 the IUCT-Oncopole was selected as a recruiter for two international studies to assess the therapeutic value of associating azacitidine with the molecule APR 246 (phase III trial, open) or a TIM3 inhibitor (CMBG453 – double-blind phase III trial). Only two or three centers in France were open for each trial.

Main collaboration: CRCT team 18 (Dr J-E. Sarry): Development of research into the influence of immuno-metabolic status on the evolution of myelodysplastic syndromes and responses to treatments (Dr T. Comont).

Selected publications in 2019 :

. Vaysse, C. et al. **Small Private Online Course in Teaching Oncology-Feedback After 1 Year: What Lessons?** J Cancer Educ (2019).
. de Swart, L. et al. **Impact of red blood cell transfusion dose density on progression-free survival in lower-risk myelodysplastic syndromes patients.** Haematologica (2019)
. Sébert, M. et al. **A phase II study of guadecitabine in higher-risk myelodysplastic syndrome and low blast count acute myeloid leukemia after azacitidine failure**. Haematologica (2019)

OCC
DIGESTIVE CANCERS

Coordinator: Prof. Rosine GUIMBAUD

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**2,596 patients (- 1.29%)**
Surgery	**647 patients (- 3.86%)**
Chemotherapy	**652 patients (+ 6.71%)**
Radiotherapy	**233 patients (+ 0.87%)**
Brachytherapy	**5 patients (+ 150%)**

14 physicians
13,633 hospital stays (+8.48% compared with 2018)
21 clinical trials ongoing, including 4 phase I/I-II trials
Collaborations with CRCT teams 2 (Dr M-J. Pillaire) and 10 (Dr P. Cordelier)

Strategic objectives: The OCC specializes in all types of digestive cancer (intestine, liver/pancreas) and all stages of cancer care from screening to diagnosis and treatment. It is a referral center for: genetic screening for colorectal/gastric and pancreatic cancers; early diagnosis of pancreatic-colorectal and liver cancers; esophagogastric, pancreatic, hepatobiliary (including transplants), rectal and peritoneal surgery; interventional radiology; systemic and intra-arterial cytotoxic therapies; and radiotherapy. Research activities center round molecular markers and genetic instability of colorectal cancers and the search for innovative therapies for pancreatic cancers.

• Since 2018 a molecular MDT has brought together the digestive cancers OCC, the molecular unit and the phase I trials department. In addition, two digestive cancer MDTs and a HCC MDT meet every week.
• Phase 2 and 3 clinical trials are always in progress and contribute to the development of new therapeutic standards.
• Projects launched in 2019 include the "Pol-E national cohort", which involves 25 French molecular biology laboratories and clinician-researchers at each site. Supported by the Francophone Digestive Cancer Federation and French "COMAD" funding, its aim is to identify and characterize tumors (digestive and non-digestive) with a mutation of the Po-E gene, and to collect samples on site.
• On a similar theme, the functional analysis of a Pol-E mutation with specific clinical value is the subject of the "ONCOPOL-E" project (@IUCT-Oncopole translational grant).
• The BACAP clinical-biological consortium, France's largest study group on pancreatic cancers, continues to be highly active and has submitted several projects to the Scientific Council. THERGAP2, an internally promoted clinical trial, to evaluate a gene therapy has been launched and is open to inclusions.

Selected publications in 2019 :

. 1. de la Fouchardière C. et al. **Characteristics of BRAFV600E Mutant, Deficient Mismatch Repair/Proficient Mismatch Repair, Metastatic Colorectal Cancer: A Multicenter Series of 287 Patients**. Oncologist. 2019 Dec;24(12):e1331-e1340.
2. van den Boorn HG, et al. **A Registry-Based Prediction Model for Overall Survival in Patients with Metastatic Oesophageal or Gastric Cancer**. Cancers (Basel). 2019 Feb 5;11(2):187.

OCC
THORACIC CANCERS

Coordinator: Prof. Julien MAZIÈRES

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**1,781 patients (- 0.17%)**
Surgery	**269 patients (- 7.24%)**
Chemotherapy	**667 patients (+ 6.55%)**
Radiotherapy	**323 patients (- 0.62%)**
Brachytherapy	**2 patients (- 100%)**

11 physicians, including 1 shared post
12,814 hospital stays (+3.94% compared with 2018)
450 new lung cancers (180 early stage and 270 advanced stage), 15 mesotheliomas and 15 thymomas
30 clinical trials open for inclusions (268 patients included)
Collaborations with CRCT teams 1 (Prof. M. Ayyoub / J-P. Delord), 3 (Prof. G. Favre), 20 (Dr S. Valitutti) and 21 (Dr V. Pancaldi)

Strategic objectives: The Thoracic Cancers OCC's activities cover several themes, including screening, early diagnosis, thoracic surgery, radiotherapy, targeted strategies and immunotherapies. Its basic research centers round improving understanding of resistance to treatment, whereas its translational research projects focus on four themes: analyzing biomarkers, liquid biopsies, resistance to anti-EGFR and managing toxicities.

• Phase II and III clinical trials on lung cancers and mesotheliomas have allowed new therapeutic standards to be drawn up for these pathologies.
• Research projects launched by the OCC in 2019 included LUNG-RESIST, whose aim is to "understand and overcome adaptive resistance to EGFR tyrosine-kinase inhibitors in lung cancer". The project's two components were awarded a PRTK-2018 grant and an @IUCT-Oncopole translational research grant.
• The IMMUNO-PREDICT immunotherapy project identified biomarkers of responses to checkpoint inhibitors and revealed the effect of expression of PDL1 on circulating tumor cells. Moreover, a collaboration with INIVATA, a leader in the field of liquid biopsies, resulted in a paper showing that it is possible to identify responders and non-responders to immunotherapy by analyzing a few key genes in a liquid biopsy.
• Another project, called LUNG PREDICT, has been 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 needed to evaluate the project's feasibility.

Selected publications in 2019 :

. Guibert, N. et al. T**argeted sequencing of plasma cell-free DNA to predict response to PD1 inhibitors in advanced non-small cell lung cancer.** Lung Cancer 137, 1–6 (2019).
. 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.** J. Clin. Oncol. JCO1901348 (2019)
. Mazières, J. et al. **Immune checkpoint inhibitors for patients with advanced lung cancer and oncogenic driver alterations: results from the IMMUNOTARGET registry**. Ann. Oncol. (2019) doi:10.1093/annonc/mdz167.
. Scherpereel, A. et al. **Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial.** Lancet Oncol. 20, 239–253 (2019).

OCC
PEDIATRIC ONCOLOGY

Coordinators: Prof. Anne LAPRIE and Dr Marie-Pierre CASTEX

Activity	Active files, excluding oral therapies (change compared with 2018)
Total	**450 patients (- 1.53%)**
Surgery	**109 patients (- 6.03%)**
Chemotherapy	**186 patients (+ 7.51%)**
Radiotherapy	**42 patients (+ 20%)**

15 physicians
3,855 hospital stays (+12.16% compared with 2018)
100 active protocols in 2019, including 37 early-phase trials
Collaborations with CRCT team 16 (coordinator: Prof. E. Delabesse) and the DEVIN team (coordinator: Dr P. Péran, UMR Inserm 1214)

Strategic objectives: The Pediatric Oncology OCC was created in 2018 as the culmination of a long-standing arrangement under which treatment is shared between 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).

• Several OCC members are members of the French Society for Children's Cancers (SFCE). Prof. A. Laprie and Dr M. Pasquet are members of the SFCE's scientific council.
• In 2019 members of the OCC contributed to regional MDT meetings within the ISOCELE inter-regional network (Toulouse, Bordeaux, Limoges), with separate MDTs for different sectors: neuro-surgery, bone tumor surgery, radiotherapy, and autologous and allogeneic bone marrow transplants. In 2020, the Occitanie and Nouvelle-Aquitaine groups will merge within the SFCE's new inter-regional structure.
• The Pediatric Oncology OCC designs and conducts numerous regional, national and European clinical research projects (100 active protocols in 2019). Two multi-center PHRC-K projects (BEACON and CURALASE) are sponsored locally. 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": Prof. A. Laprie coordinates the radiotherapy work package of the Multi-Regional Research On Brain – Optimized Therapy ("MrROBOT") program and coordinates the IMPALA prospective study on radiotherapy's impact on the memory, for which inclusions began in February 2020. For the last four years, she has also coordinated the PEPPI multi-center study on childhood ependymoma.
– "Leukemias": The OCC contributes to the "Connect AML" PAIR project, sponsored by Dr M. Pasquet, whose aim is to better understand the early development of acute myeloblastic leukemia (AML).

Selected publications in 2019 :

. Janssens, G. O. et al. **Recommendations for the organisation of care in paediatric radiation oncology across Europe: a SIOPE-ESTRO-PROS-CCI-Europe collaborative project in the framework of the JARC**. Eur. J. Cancer 114, 47–54 (2019).
. Noirrit-Esclassan, E. et al. **Photobiomodulation with a combination of two wavelengths in the treatment of oral mucositis in children: The PEDIALASE feasibility study**. Arch Pediatr 26, 268–274 (2019)
. Tensaouti, F. et al. **Feasibility of Dose Escalation in Patients With Intracranial Pediatric Ependymoma**. Front Oncol 9, 531 (2019).

Medico-technical services

Twelve medico-technical departments provide support for the Organ Co-ordination 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
37,933 procedures (-0.21% compared with 2018) including 12,060 nuclear medicine procedures, 9,049 TDM scans, 4,372 MRI scans, 5,777 x-rays, 2,515 ultrasound scans

. 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. As part of the National Authority for Health's quality initiative, a collaborative project (coordinated by B. Lucas and V. Bouyssou) has been launched to review processes within the three services and interactions between the Medical Imaging Department and the Medical Physics, Hospitalization and Radioprotection Departments, notably by holding periodic multidisciplinary meetings ("chats"). This initiative has strengthened cohesion and improved communication. In addition, work has begun to strengthen the department's collaborations with the independent sector by creating a shared patient ID server, an objective that is supported by Occitanie Regional Health Agency.

. The Medical Imaging Department's PET center has been awarded the European Association of Nuclear Medicine's "European Center of Excellence" label every year since 2015. This accreditation, which recognizes the high quality of the center's work in terms of patient care and the examinations it carries out, facilitates participation in European research protocols, such as those sponsored or coordinated by the European Organisation for Research and Treatment of Cancer.

. The European Neuroendocrine Tumor Society's certification of the IUCT-Oncopole and the IUCT-Rangueil/Larrey as a "European Centre of Excellence for Neuroendocrine Tumors" encompasses the Medical Imaging Department. Accreditation was granted following an audit of the two institutes that was steered by Prof. R. Guimbaud and Dr L. Dierickx. The newly certified unit is called the "Toulouse University Centre Of Excellence for Neuroendocrine Tumors".

. Important purchases in 2019 included a stereotactic breast biopsy unit (tomosynthesis/3D mammography) and several specialist software packages to improve safety and quality. In addition, routine use of the second PET scanner, acquired at the end of 2018, has reduced waiting times for patients. Finally, in 2020 the department will increase its interventional radiology capabilities when it replaces its existing scanner with a new machine incorporating several new technologies.

. Other measures to improve patient care include expanding the accessibility of new tracers and introducing a specialist consultation in angiologia and vascular medicine (echography).

. In addition, the department is examining the possibilities offered by artificial intelligence, most notably via a project to "train" a computer to recognize tumors from PET images, which was launched by Dr S. Kanoun in 2019. 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 (project to develop a method to automatically contour structures for radiotherapy, in collaboration with Dr S. Ken and Dr L. Simon).

Selected publications in 2019 :

. Voglimacci, M. et al. **Chemoradiotherapy for locally advanced cervix cancer without aortic lymph node involvement: can we consider metabolic parameters of pretherapeutic FDG-PET/CT for treatment** tailoring? Eur. J. Nucl. Med. Mol. Imaging (2019)

. Puszkiel A, et al. **Evaluation of the Interaction of Amino Acid Infusion on 177Lu-Dotatate Pharmacokinetics in Patients with Gastroenteropancreatic Neuroendocrine Tumors**. Clin Pharmacokinet. (2019)

. Ploussard G, et al. **Value of Concomitant Systematic and Fusion Targeted Biopsies for Grade Group Prediction Based on Radical Prostatectomy Final Pathology on Positive Magnetic Resonance Imaging**. W. J. Urol. (2019)

. Leenhardt L, et al. **Recombinant Thyrotropin vs Levothyroxine Withdrawal in 131I Therapy of N1 Thyroid Cancer: A Large Matched Cohort Study (ThyrNod).** Clin Endocrinol Metab. (2019)

Nuclear Medicine and Brachytherapy Hospitalization Unit

Unit head: Prof. Isabelle Berry
1,010 hospital stays, excluding treatment sessions (-8.8% compared with 2018) but
including 225 brachytherapy stays (+15.4%) and 589 SIRT stays (+7.3%)

. France's largest vectorized internal radiotherapy unit has 18 individual rooms with video monitoring and background radiation measurement. Thirteen of these rooms (including 3 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 has shortened hospital stays 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 every patient receives the best possible care.
. The number of 5-day hospitalization patients was similar in 2019 to 2018 due to a reduction in indications for micro-treatments for the thyroid. In contrast, the number of day hospitalizations fell markedly because of a decrease in the number of these checks and because they are now conducted at longer intervals. The reduced reimbursement rate for treating bone metastases of prostate cancer has played a part, but the imminent arrival of new molecules should lead to these figures increasing in 2020.
. The unit is a regional brachytherapy referral center, mostly for gynecological cancers, although the IUCT-Oncopole has also provided high dose-rate brachytherapy for prostate cancer since 2016. Almost two-thirds (64%) of the unit's activity centers round treating thyroid cancers, work that is carried out in collaboration with Prof. F. Courbon and Dr S. Zerdoud. However, its inpatient activity is becoming more varied and now includes treating bone metastases of prostate cancer and, more recently, neuroendocrine cancers, which have been treated on a routine basis, under the impulsion of Dr L. Dierickx, since clinical trials were successfully completed in 2017. In 2019, 83 hospital stays at the IUCT-Oncopole were for neuroendocrine cancers (+15.3% compared with 2018).
. The GENBIOLuNET project, led by Dr L. Vija Racaru, was launched in 2019 thanks to a GIRCI-SOHO grant. It involves measuring variability in molecular biomarkers that can be used to monitor radio-nucleotide therapies (Lu-177 DOTATATE) administered to patients with metastatic neuroendocrine tumors of the stomach and lower intestine.

Operating suite

Head of department: Prof. Sébastien Vergez
Assistant head: Dr Alejandra Martinez
7 operating rooms, including one devoted to R&D
5,299 patients (+1.81% compared with 2018)
7,548 operations (-1.99% compared with 2018), 2,511 of which were to fit or remove a port or a CVC (-5.06% compared with 2018)

. 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 innova-

tive 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).
. In its 2019 survey of French hospitals, Le Point magazine ranked the IUCT-Oncopole 3rd for head and neck cancer surgery (5th in 2018), 5th for breast cancer surgery (3rd in 2018) and 6th for gynecological cancer surgery (also 6th in 2018).
. In 2019 the department 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. Fourteen patients have followed the program.

Anesthesiology Unit

Manager: Dr Sébastien Pierre
4,566 consultations and 3,934 patients (–0.48% and +0.92%, respectively, compared with 2018)
4,975 anesthesia procedures of all kinds except local (+2.19% compared with 2018)

. In addition to providing anesthesiology services to all the IUCT-O's departments, the unit is responsible for providing medical care to patients in the surgery department. It also works with the quality improvement service on improving communication between stakeholders.
. 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.
. The Anesthesiology Unit, in collaboration with the Sport Médipole clinic's anesthesiology-intensive care department, hosted the first Regional Meeting of Anesthesiology Units in November 2019. Focusing on perioperative rehabilitation, the event attracted around 50 anesthesiologists and nurse anesthetists from throughout the Occitanie region.
. Dr P. Izard and Dr R. Fuzier are members of the Interest Group on Human Factors in the Field of Health (GIFH), a multidisciplinary group of medical-surgical and paramedical healthcare professionals, risk-management specialists, and other professionals who deal with risk (air traffic controllers, pilots, etc.). GIFH's aim is to improve the quality and safety of healthcare. Two innovative initiatives launched in 2019 brought together perspectives on risk from the healthcare and civil aviation sectors. The first initiative was a training course for anesthesia professionals, entitled "Minimize human-related risks in health care: learn to fly!", which used experiences in the aviation sector to examine risks arising from human factors. The course's two sessions addressed routine tasks and emergency situations. The second initiative, entitled "Dr Captain Time", consisted of a series of short videos, posted on our websites and on social media, examining a variety of risks relating to forgetting tasks and possible solutions drawn from aviation. These two initiatives were presented at a half-day workshop called "People at the heart of risk management",

held by Unicancer in October 2019. In addition, at the beginning of 2020, medical personnel will be given the opportunity to do a specially adapted Crew Resource Management training session on the Airbus A320 simulator.
. Dr S. Leclerc and Dr A. Martinez are members of Unicancer's "Accelerated Rehabilitation After Cancer" group. In 2019 they helped prepare the group's next annual meeting, which will be hosted by the IUCT-Oncopole in 2020.
. Since 2019 Dr R. Fuzier has helped draw up European guidelines on vascular access and ultrasound-guided local-regional anesthesia. They will be published in the European Journal of Cancer in 2020.
. In terms of research, 2019 saw the completion of the DCPO Sein Mineur observational study to assess the effect of preoperative thoracic block (ultrasound-guided injection of local anesthetic around the serratus muscle) on the prevalence of chronic pain three months after conservative breast cancer surgery. Results of the study, which included 250 patients, will be published in 2020.

Selected publication in 2019 :

. Fuzier, R., Izard, P., Daboussi, A., Pouymayou, J. & Pierre, S. **A case report of sustained resolution of cancer pain by continuous perineural infusion of local anaesthetic**. Eur J Pain 23, 31–34 (2019).

Intensive and Intermediate Care

Manager: Dr Jean Ruiz
12 beds
476 patients (+0.6% compared with 2018) and 624 admissions, including 424 from the IUCT-Oncopole (surgery: 45.4%, hematology and internal medicine: 16%, medical oncology: 9.7%)
Mean length of stay: 5.57 days

. "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 Inter-

mediate Care Department, which has been a member of the program since 2014, 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.

. Several research projects are ongoing, notably in collaboration with the Respiratory Intensive Care in Onco-Hematology Research Group (GRRR-OH). 2018 saw the launch of two projects on pneumocystosis (one with the Hôpital Saint-Louis, the other with the Toulouse Institute of Federative Biology 's parasitology and mycology laboratory), as well as a project on drepanocytosis (in collaboration with Henri Mondor University Hospitals).

. 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 LATOld, this multi-center study involves eight intensive care departments across France and will include 900 patients.

Selected publication in 2019 :

. Angeles, M.A., Quenet, F., Vieille, P., Gladieff, L., Ruiz, J., Picard, M., Migliorelli, F., Chaltiel, L., Martínez-Gómez, C., Martinez, A., Ferron, G., 2019. **Predictive risk factors of acute kidney injury after cytoreductive surgery and cisplatin-based hyperthermic intra-peritoneal chemotherapy for ovarian peritoneal carcinomatosis**. Int. J. Gynecol. Cancer. (2019)

Radiotherapy Department

Head of department: Prof. Elizabeth Moyal
Assistant head: Dr P. Graff-Cailleaud
58,107 radiotherapy sessions, 79.8% of which were IMRT
50 total body irradiation sessions (+38.89% compared with 2018)

. The Radiotherapy Department keeps fully up to date with innovations and advances in treatment. For example, in 2017 it became the first center in France to provide adaptive tomotherapy and in 2018 it received its eighth high flow rate bunker. Moreover, as a way of reducing patients' anxiety about radiotherapy, since 2017 the department has offered the option of receiving treatment under hypnosis. 2019 saw the introduction of moderately hypofractionated schedules for treating prostate cancer.

. The department was one of the instigators of RADIOTRANSNET, an INCa-accredited national network for structuring preclinical research in radiotherapy that was launched in 2018 (Prof. E. Moyal is a member of the steering committee). By facilitating interactions between basic, translational and preclinical research at the interface between radiotherapy and radiobiology, RADIOTRANSNET will help define strategic priorities in the search for innovative radiotherapy techniques and technologies.

. As a result, the department is highly involved in both clinical and upstream translational research in radiobiology (close links with CRCT team 11), as well as in metabolic and functional imaging for radiotherapy. It contributes to several projects coordinated by the OCCs and runs numerous trials and research projects.

. Several projects combining radiotherapy with immunotherapy were launched in 2019:

- 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.

- CITHARE is the first prospective randomized clinical trial entirely devoted to patients with a cancer of the oropharynx of viral origin. Coordinated by Dr A. Modesto in collaboration with the Head and Neck OCC, inclusions began in 2018 and will continue until the end of 2020.

- SI2GMA (sponsored by Prof. E. Moyal), funded by a Regional Health Agency SIGN'IT grant, examines predictive factors for responses to combined radiotherapy-immunotherapy for recurrent glioblastoma.

- SILK (coordinated by Prof. E. Moyal) is a trial to evaluate the effectiveness of combining radiotherapy with immunotherapy in lung cancer patients with brain metastases.

. Following the award of a PHRC 2018 grant, the BLAD-RAD01 project (sponsored by Dr J. Khalifa) was launched in 2019. BLAD-RAD01 will assess the efficacy of consolidative radiotherapy in patients with a metastatic urothelial carcinoma of the bladder. The first patients will be included in 2020.

. In addition, the Booster Melanoma study, coordinated by Dr Chira and Dr C. Gomez Roca, continues to include patients. It examines the immune-mediated abscopal effect of stereotactic radiotherapy in patients with melanomas. Results should be known by 2024.

. Finally, in 2019 the Radiotherapy and Medical Physics Departments, in collaboration with Varian Medical Systems, launched a project called COBRA to develop a new tool to optimize treatment while preserving organs at risk, especially in the case of neurological tumors. .

Selected publications in 2019 :

. Covin, B. et al. **Refining the risk-stratification of transrectal biopsy-detected prostate cancer by elastic fusion registration transperineal biopsies**. World J Urol 37, 269–275 (2019).

. Deshors, P. et al. **Ionizing radiation induces endothelial transdifferentiation of glioblastoma stem-like cells through the Tie2 signaling pathway**. Cell Death Dis 10, 816 (2019).

. Laprie, A. et al. **Dose-painting multicenter phase III trial in newly diagnosed glioblastoma: the SPECTRO-GLIO trial comparing arm A standard radiochemotherapy to arm B radiochemotherapy with simultaneous integrated boost guided by MR spectroscopic imaging.** BMC Cancer 19, 167 (2019).

Pharmacy

Manager: Dr Jean-Marie Canonge
Assistant manager: Dr Florent Puisset
France's largest cancer hospital pharmacy in terms of chemotherapy preparations.
130,000 chemotherapy preparations, consisting of 117,000 standard chemotherapy preparations and 13,000 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 Santé Relais Domicile.
48,000 anticancer chemotherapy prescriptions
148 pharmaceutical consultations and 563 medication reconciliations for oral anticancer drugs

. The number of preparations dispensed by the Pharmacy continued to grow in 2019, with a 7% increase in IV chemotherapy preparations and a 13% increase in the quantity of oral anticancer drugs dispensed. The number of preparations produced for clinical trials also increased by 13% in 2019.
. The Pharmacy further improved the safety of its preparation circuit by introducing video monitoring of chemotherapy preparation procedures for both standard and clinical trials preparations. This innovative system, called Drug Cam, uses image processing techniques to check the most critical stages of the preparation process. Drug Cam monitors 50% of production for standard chemotherapy preparation and 100% of production for clinical trials preparations.
. In October 2019 Occitanie Regional Health Agency approved the launch of CAR-T cell therapy (IUCT-Oncopole Pharmacy and Hematology Department). Eight patients received this innovative therapy in 2019.
. The consultation and medication reconciliation process for patients being discharged that was launched in 2015 following the introduction of oral therapies, was extended in 2018 by including more time to address pharmaceutical isssues. This system ensures close links between the hospital and family doctors/pharmacies in order to reduce the risks from drug interactions. Despite having limited resources, the Pharmacy managed to expand this system in 2019. However, further expansion will be difficult, despite the large increase in the use of oral therapies.
. In addition, the Pharmacy has further developed 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.
. Moreover, in October 2019 the IUCT-Oncopole, via Toulouse University Hospital, was chosen to take part in the "Expensive Molecules" experiment launched under Article 51 of the 2018 Social Security Financing Act (60% of the data will be supplied by the IUCT-Oncopole's pharmacy). The experiment will begin in 2020 and last three years.
Finally, as part of a hospital-university cooperation program launched by Toulouse University Hospital in 2015, the IUCT-Oncopole's pharmacy advised Vietnam's National Cancer Center on transposing Toulouse's centralized chemotherapy preparation model to Hanoi. Vietnam's first centralized unit opened in 2019. Moreover, the Pharmacy was invited to take part in the Cancer Centers of Vietnam's annual congress, from 27th to 29th November 2019.

Selected publications in 2019:

. Paludetto MN, Puisset F, Chatelut E, Arellano C. **Identifying the reactive metabolites of tyrosine kinase inhibitors in a comprehensive approach: Implications for drug-drug interactions and hepatotoxicity**. Med Res Rev. 2019 Nov;39(6):2105-2152
. Puisset F, Bigay-Game L, Paludetto MN, Martel A, Perriat S, Rabeau A, Canonge JM, Mazieres J. **Safety of oral hydration after cisplatin infusion in an outpatient lung cancer unit**. Support Care Cancer. 2019 May;27(5):1679-1686

Oncology Medical Biology Laboratory (LBMO)

Coordinator: Prof. Gilles Favre

. 783,177 examinations (-0.52% compared with 2018) and 8,257,011 class-B procedures: (-1.72% compared with 2018)
. 56.95% increase in RIHN[1] procedures compared with 2018, including oncogenetics: 11,504,380 (+76.6% compared with 2018), prospective biology: 678,150 (-28.78% compared with 2018), pharmacology: 388,130 (+3.44% compared with 2018) and rapid-response biology (immuno-assays, biochemistry): 62,810 (-32.27% compared with 2018)

. The COFRAC-accredited 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). 98% of the Laboratory's activities are accredited by France's accreditation agency (COFRAC).
. In addition to its routine work, the LBMO contributes to translational studies in collaboration with the CRCT's research teams. In fact, four of the LBMO's managers are also the heads of CRCT research teams: Prof. M. Ayyoub: team 1, Prof. G. Favre: team 3, Dr C. Toulas: team 11, and Prof. E. Chatelut: team 14. In 2019 the LBMO contributed to a study to refine the spectrum of tumor mutational load that needs to be evaluated before immunotherapy. Results, published in Lung Cancer, showed that it was necessary to sequence only a small number of target genes to predict responses to therapies targeting the PD 1 immunity checkpoint inhibitor. This study was conducted in collaboration with the Prospective Biology Unit, which has been carrying out real-time studies of circulating molecules since 2018.
. The LBMO also conducts its own research projects, such as the project launched in 2019 by the Oncogenetics and Pharmacogenetics Unit to identify bowel cancer genes in young patients (below the age of 40). Furthermore, at the beginning of 2019 the Pharmacology Unit published the results of the PHACS (Pharmacokinetics of Tamoxifen and Anti-aromatases, Correlation with Pharmacogenetic Characteristics) study, which included more than 2,000 patients. Other research projects are being conducted within Unicancer's Genetics and Cancer group.
. The LBMO also takes part in clinical studies in collaboration with the Clinical Trials Office. To meet these growing needs, a full-time post has been created to manage samples taken during clinical trials at the IUCT-Oncopole. Nationwide studies in which the LBMO is involved include COVAR (classify variants of cancer susceptibility genes whose signification is unknown), TUMOSPEC (identify breast and ovarian cancer susceptibility genes other than BRCA) and GREAT (study the genes involved in ovarian tumors' responses to PARP inhibitors).
. In 2019 the Oncogentics and Pharmacogenetics Unit 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 collaboration with the Pathology Laboratory), have received COFRAC accreditation. 2019 also saw the introduction of testing for the the TP53 gene prior to radiation therapy

for all women with breast cancer and a rapid BRCA test protocol for ovarian cancers.

. The Immune Monitoring Unit was created in 2017 to support the work being carried out by IUCT-Oncopole clinicians to develop immunotherapies. The unit's main objective is to identify the biological parameters underlying responses to the toxicity of immunotherapies and thereby help clinicians prescribe the most appropriate therapies. As well as supervising patients receiving treatment, the unit provides specialist monitoring for immunotherapy clinical trials, such as the MINER trial, which was launched in 2018 by the IUCT-Oncopole with support from the imCORE network and the MSD Avenir foundation. The unit contributes to this trial by monitoring immunological mechanisms and biomarkers that can be used to assess the effectiveness and toxicity of immunotherapy treatments for different cancers (melanomas, lung cancer, bladder cancer, head and neck cancers, etc.). In addition, the unit launched several new trials in 2019 to build on research carried out by CRCT team 1.

. Furthermore, the LBMO actively contributes to the development of new approaches and technologies via partnerships with biotechnology startups and innovative companies, such as Picometrics. Another of these startups, Smartcatch, whose objective is to develop an in-vivo CTC capture system, is based in the LBMO, which facilitates access to blood samples and stimulates collaboration.

Selected publication in 2019:

. Chatelut, E., Le Louedec, F. & Milano, G. Setting the Dose of Checkpoint Inhibitors: **The Role of Clinical Pharmacology**. Clin Pharmacokinet (2019).

Guibert, N. et al. **Targeted sequencing of plasma cell-free DNA to predict response to PD1 inhibitors in advanced non-small cell lung cancer**. Lung Cancer 137, 1–6 (2019).

. Puszkiel, A. et al. **Factors affecting tamoxifen metabolism in breast cancer patients; preliminary results of the French PHACS study (NCT01127295)**. Clin. Pharmacol. Ther. (2019).

. Vande Perre P, Siegfried A, Corsini C, Bonnet D, Toulas C, Hamzaoui N, Selves J, Chipoulet E, Hoffmann JS, Uro-Coste E, Guimbaud R. **Germline mutation p.N363K in POLE is associated with an increased risk of colorectal cancer and giant cell glioblastoma**. Fam Cancer. 2019 Apr;18(2):173-178.

Hematology Laboratory

Manager: Prof. Eric Delabesse
33.8 million procedures

. The Hematology Laboratory carried out 56.7 million procedures in 2019, an increase of 13% compared with 2018 (+55% since 2014), in three main fields (cellular hematology, hemostasis, and onco-hematology) combining biological and clinical acts. These three fields are divided into 13 separate 13 workflows at the Purpan, Rangueil and IUCT-Oncopole sites.

. Onco-hematological analyses are performed by the Onco-Hematology Transfer Platform, which comprises the hemopathy genetics unit and myeloma genome unit. The Plat-

form performed 33.8 million procedures in 2019 (+27%; +154% since 2014), split between the hemopathy genetics unit (19.2 million procedures) and the myeloma genome unit (14.6 million procedures). Molecular and cytometric analyses were the main growth areas with numerous analyses carried out for outside organizations: 51% of the analyses performed by the Hematology Laboratory in 2019 (28.7 million out of 56.7 million procedures) were invoiced outside the IUCT-O, mostly to the Onco-Hematology Transfer Platform (14 million procedures for the myeloma genome unit, 12.8 million procedures for the hemopathy genetics unit).

. The laboratory is a referral center for four treatment protocols: GRAALL (adult acute lymphoblastic leukemia), CAALL-FOI (childhood acute lymphoblastic leukemia), FILO (adult acute myeloid leukemia) and IFM (French myeloma network). It contributes to numerous registers, observatories, working groups, national biological collections, and research-specific biological collections.

. The laboratory has an international reputation for its clinical research, especially the work it carries out in collaboration with CRCT teams 8 (Dr. S. Manenti), 13 (Prof. H. Avet-Loiseau), 16 (Prof. E. Delabesse) and 18 (Dr. J-E. Sarry).

Selected publication in 2019:

. 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, Hebraud 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. 2019.

. Largeaud L, Berard E, Bertoli S, Dufrechou S, Prade N, Gadaud N, Tavitian S, Bories P, Luquet I, Sarry A, De Mas V, Huguet F, Delabesse E, Recher C. **Outcome of AML patients with IDH2 mutations in real world before the era of IDH2 inhibitors**. Leuk Res. 2019;81:82-7.

. Perrot A, Lauwers-Cances V, Tournay E, Hulin C, Chretien ML, Royer B, Dib M, Decaux O, Jaccard A, Belhadj K, Brechignac S, Fontan J, Voillat L, Demarquette H, Collet P, Rodon P, Sohn C, Lifermann F, Orsini-Piocelle F, Richez V, Mohty M, Macro M, Minvielle S, Moreau P, Leleu X, Facon T, Attal M, Avet-Loiseau H, Corre J. **Development and Validation of a Cytogenetic Prognostic Index Predicting Survival in Multiple Myeloma**. J Clin Oncol. 2019;37(19):1657-65.

Pathology Laboratory

Director: Prof. Pierre Brousset
Assistant directors: Prof. Emmanuelle Uro-Coste and Dr Philippe Rochaix
61,238 cases, including 21,365 external requests
77,151 examinations and 70,204 reports sent to prescribers
457,883 slides read and 237,533 paraffin blocks created, including 64,347 for biopsies
Publications - SIGAPS score: 784
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, 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); and rare neuroendocrine tumors – TENpath (Dr Marie Danjoux). It is also a national coordinator, alongside Creteil, for the Lymphopath network (12,000 cases per year).

. 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 into lymphomas. Prof. Laurent, in collaboration with Dr S. Kanoun, is currently coordinating a machine learning project on microscopy and PET-scan images.

. 2019 saw the completion of a major project, sponsored by Dr M. Colombat in collaboration with the Institute of Pharmacology and Structural Biology (IPBS - coordinator: Dr O. Burlet-Schiltz), to develop a new typing technique involving mass spectrometry proteomic analysis of amyloses (developed in 2009 by an American team). As a result, the IUCT-O, through its Pathology Laboratory, has become a European reference center for typing amyloses, a rare and complex disease characterized by abnormal deposition of proteins in tissues. One of Dr M. Colombat's papers on proteomics was featured on the cover of Blood in 2019.

. Blood featured another LBMO paper on the cover of its November 2019 issue. This paper, by Prof. C. Laurent, addressed the molecular decoding of large-cell anaplastic lymphoma associated with textured breast implants.

. LabEx TOUCAN, which focuses on hematopoietic cancers, has been renewed for five years. During its first five years, LabEx TOUCAN produced 230 papers (with an h-index of 40), filed several patents, created startups (ongoing), and strengthened ties with Laboratoires Pierre Fabre and ROCHE. Funding provided by the program's renewal will be used to create AI applications for the Imaging Unit and to develop single-cell RNA sequencing (scRNA-seq), in conjunction with CRCT team 9 (coordinator: J-J Fournié), to evaluate tumor heterogeneity and the resistance of lymphoid sub-populations in the microenvironment.

. The main AI projects envisaged within the TOUCAN program will examine:

- Using unsupervised machine learning to characterize grade-2 breast cancers, in collaboration with Unicancer and Thalès Services (project sponsored by Dr C. Franchet),
-Using analyses of histology images to predict the characteristics of large-cell B lymphomas (project sponsored by Prof. C. Laurent and Prof. L. Ysebaert).

. In addition, a collaboration between CRCT team 20 (coordinator: Dr S. Valitutti), the Imaging Unit and Pathology Laboratory has been set up to use machine learning to develop a computerized system for analyzing complex functional microscopy images (multiplex immunofluorescence).

. Also in 2019 a partnership was signed 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 & 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. This project is co-sponsored by Dr C. Syrykh and Dr C. Franchet.

. Finally, the Pathology Laboratory is working to obtain quality certification, notably for its molecular biology activities. The first steps in this process were taken in 2018.

Selected publications in 2019:

. Camus, M. et al. **Proteomics evidence of specific IGKV1-8 association with**

cystic lung light chain deposition disease. Blood (2019).
. Laurent, C. et al. **Gene alterations in epigenetic modifiers and JAK-STAT signaling are frequent in breast implant-associated ALCL.** Blood (2019).
. Siegfried, A. et al. **EWSR1-PATZ1 gene fusion may define a new glioneuronal tumor entity.** Brain Pathol. 29, 53–62 (2019).
. Vendrell, J. et al. **Ultra-sensitive EGFRT790M detection as an independent prognostic marker for lung cancer patients harboring EGFRdel19 mutations and treated with first-generation TKIs.** Clin. Cancer Res. (2019)

Cancer BioBank (CRB cancer)

Manager: Prof. Anne Gomez-Brouchet
270 m² of dedicated space
33 collections
75,944 samples (tumor and non-tumor samples), +11.7% compared with 2018
6,457 new samples and 11,500 samples provided to research teams

. One of the Cancer BioBank's key roles 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).
. In order to raise its profile, the Cancer BioBank has begun the process of obtaining ISO 9001 certification (in addition to the NF-S-96 900 certification already obtained). The Organisation of European Cancer Institutes (OECI) recognized the quality of the Cancer BioBank's work when it audited the IUCT-Oncopole in December as part of the Comprehensive Cancer Center accreditation process. The OECI's auditors singled-out the Cancer BioBank as one of the Oncopole's strengths.
. The Cancer BioBank has responded to a demand from researchers and commercial partners by consolidating the links between the site's different units and the university hospital. Actions taken include creating a "block library" (for the colon, lung, breast and kidney collections) and supplying fresh tissues (in collaboration with the Pathology Laboratory), annotating the main collections, including the multi-center pancreatic adenocarcinoma collection (INCa-BACAP), and creating new liquid collections (bladder, lungs). In 2020, the Cancer BioBank will receive another major collection in the form of the "animal" collection from Toulouse University Hospital's IHU INSPIRE project. It also aims to become the CRCT's histopathology unit in order to provide its research teams with the various types of tissue sample they need for their research.
. The Cancer BioBank contributed to 56 research projects in 2019 (28 involving the Institute's partners and 28 with external academic and industrial partners) and 41 clinical trials (compared with 25 in 2018).
. In 2019 the Cancer BioBank extended many of its long-standing partnerships with commercial companies, most notably with Laboratoires Pierre Fabre and EVOTEC.
. Several papers arising from studies to which the Cancer Bio Bank contributed were published in 2019.

Selected publications in 2019:

. Nicolle, R. et al. **Integrated molecular characterization of chondrosarcoma reveals critical determinants of disease progression**. Nat Commun 10, 4622 (2019).
. Zamora A, et al. **Paclitaxel induces lymphatic endothelial cells autophagy to promote metastasis**. Cell Death Dis. 2019 Dec 20;10(12):956.

Engineering and Medical Physics Department (DIPM)

Manager: Régis Ferrand
3,285 doses calculated in 2019
2,768 doses calculated by the Biomedical Engineering Unit

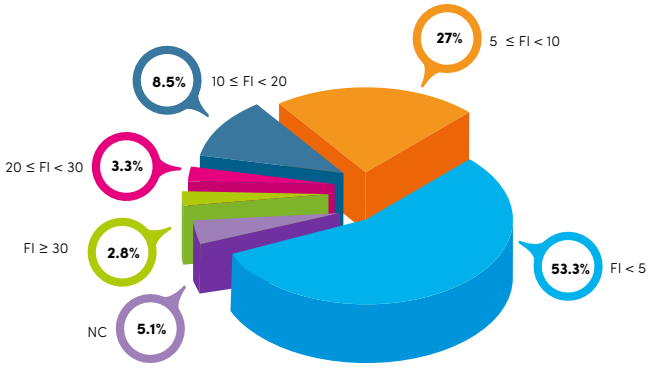
. The Engineering and Medical Physics Department (DIPM) consists of a Medical Physics Unit and a Biomedical Engineering Unit. It supports the IUCT-Oncopole's clinical and research activities by installing and maintaining biomedical equipment and by ensuring, via the Medical Physics Unit, that equipment 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 radiation therapy treatments (patient quality, dosimetry for external radiation therapy, brachytherapy and internal radiation therapy) and carries out research within the unit through CRCT team 15, which includes several clinicians.
. Moreover, since 2018 Dr S. Ken has been an associate researcher with the Institute of Computer Research's Computational Imaging and Vision (MINDS) team (coordinator: Dr A. Basarab), where he helps develop advanced image analysis and interpretation tools.
. 2019 was an active year in every area, notably due to major changes in software infrastructure both for the Biomedical Engineering Unit, with the introduction of a new maintenance management tool for the entire site, and for radiotherapy physics.
. In addition, two multi-annual, collaborative projects were launched in 2019 to develop new pieces of equipment. The first project, conducted in conjunction with General Electric focuses on imaging and includes an "Industrial Contracts for Training through Research" (CIFRE) doctoral project. The second project is a collaboration with Varian Medical Systems in the field of radiation therapy.
. Several translational research projects, conducted in collaboration with teams in the "hard sciences", were launched or continued in 2019. For example, a project to model beams in radiation therapy is being run in collaboration with medical physics teams from Catalonia and the Institut Sainte Catherine in Avignon (three papers in international journals to date and ongoing grant applications). The Department also contributes to the Computreat project, in conjunction with the Toulouse Institute of Mathematics (IUCT-Oncopole coordinator: Prof. L. Ysebaert), and to the European Medirad project (dosimetry in vectorized internal radiation therapy - IUCT-Oncopole coordinator: Prof. F. Courbon).
. The department's collaboration with Brain Lab to ensure more precise patient positioning for intra-cranial stereotactic treatment came to an end in 2019. On the other hand, the department has extended its collaboration with Oléa Medical and has begun a new collaboration with a small Toulouse company, called JoliBrain, to apply AI to 4D scanners.

IV

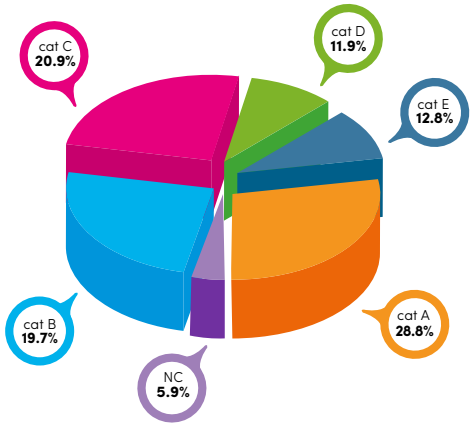
VALORIZATION

Publications

The IUCT-Oncopole's basic, translational and clinical research activities gave rise to **633** publications in 2019 (**+11%** compared with 2018) in **296** journals (**41%** with an A or B SIGAPS ranking). The mean impact factor (2018 value, excluding NC*) was **7.174** in 2019 (compared with **7.06** in 2018).



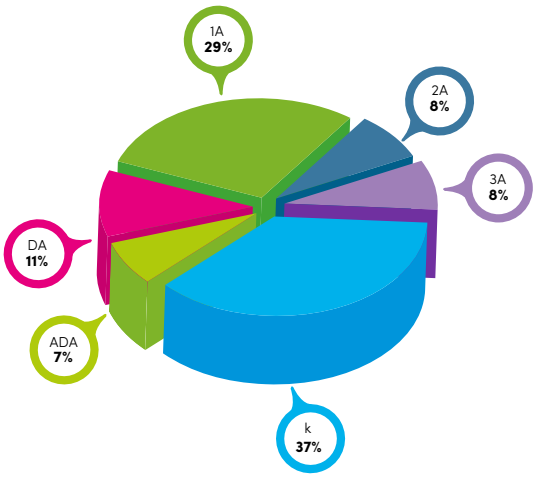
Percentage of papers by impact factor



Percentage of papers by SIGAPS category (exc. NC*)

International journals in which the IUCT-Oncopole published papers in 2019

Blood
Journal of Clinical Oncology
The New England Journal of Medicine
Annals of Oncology
Lancet Oncology
JAMA Oncology
Nature Communications



Percentage of papers by author position

Papers published in journals with an impact factor greater than 10 are listed in an appendix at the end of this report. A full list of papers published in 2019 by the IUCT-Oncopole can be found at our website:
https://www.iuct-oncopole.fr/publications-scientifiques

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

Patents

16 patents were published in 2019.

N° publication	Date de publication	Titre	Demandeurs
EP3579872A1	18/12/2019	Methods and pharmaceutical compositions for the treatment of cancers associated with activation of the MAPK pathway	Inserm, University of Toulouse III—Paul Sabatier, Toulouse University Hospital
EP3555626A1	23/10/2019	Methods and kits for detecting basophil activation	Inserm, University of Toulouse III—Paul Sabatier, CNRS, Université de Stanford
WO2019162325A1	29/08/2019	Use of sk1 as a biomarker for predicting response to immune checkpoint inhibitors	Inserm, University of Toulouse III—Paul Sabatier, Toulouse University Hospital
EP3530758A1	28/08/2019	Method for determining the in vitro presence of a target molecule in a biological sample, and its use for the in vitro analysis of cancers, in particular soft-tissue sarcomas and gastrointestinal stromal tumors	Université de Bordeaux, Inserm, Institut Bergonié, University of Toulouse III—Paul Sabatier, Institut Claudius Regaud
WO2019158512A1	22/08/2019	Methods for the prognosis and the treatment of glioblastoma	Inserm, University of Toulouse III—Paul Sabatier, Institut Claudius Regaud
WO2019149736A1	0808/2019	Method to predict the need for therapy of patients suffering from chronic lymphocytic leukemia	Inserm, University of Toulouse III—Paul Sabatier, CNRS, Toulouse University Hospital
EP3515453A1	31/07/2019	Methods and pharmaceutical compositions for reprograming immune environment in a subject in need thereof	Inserm, University of Toulouse III—Paul Sabatier, Affichem
EP3491387A1	05/06/2019	Methods of treatment of cancer disease by targeting tumor associated macrophage	Inserm, University of Toulouse III—Paul Sabatier, CNRS
EP3491022A1	05/06/2019	Antibodies targeting tumor associated macrophages and uses thereof	Inserm, University of Toulouse III—Paul Sabatier, CNRS, Toulouse University Hospital, Institut Claudius Regaud
WO2019101871A1	31/05/2019	A new marker for predicting the sensitivity to pi3k inhibitors	Inserm, University of Toulouse III—Paul Sabatier, CNRS
WO2019073031A1	18/04/2019	Combination treatment of pancreatic cancer	Inserm, University of Toulouse III—Paul Sabatier, CNRS, Klinikum Rechts der Isar der Technischen Universitat Muenchen
WO2019057649A1	28/03/2019	Methods and pharmaceutical compositions for the treatment of acute myeloid leukemia	Inserm, University of Toulouse III—Paul Sabatier, Toulouse University Hospital
EP3452092A1	13/03/2019	Pharmaceutical compositions for the treatment of chemoresistant acute myeloid leukemia (AML)	Inserm, University of Toulouse III—Paul Sabatier, CNRS, Toulouse University Hospital
EP347068A1	27/02/2019	Synthetic single domain antibody	Inserm, Institut Curie, University of Toulouse III—Paul Sabatier, CNRS
EP3429597A1	23/01/2019	Cytidine deaminase inhibitors for the treatment of pancreatic cancer	Inserm, University of Toulouse III—Paul Sabatier
WO2019008136A1	01/01/2019	Transducer for the monitoring of metabolic status of a biological entity	Inserm, CNRS, University of Toulouse III—Paul Sabatier

Knowledge sharing

1,246 students, including 176 interns and 71 doctoral students
37 nationalities
110 IUCT-Oncopole clinicians provide teaching
14 associated master's degrees, including the University of Toulouse III—Paul Sabatier Master's in Cancerology
24 vocational training courses plus 9 university and inter-university diplomas
66 medical-scientific events, including 56 organized by the IUCT-Oncopole

Simulation-based initial training

Simulation-based training for caregivers and input from users

• Following its introduction in 2018, simulation-based training was rolled out across both of Toulouse's faculties of medicine in 2019. As a result, 280 graduate students practiced invasive examinations on mannequins and developed their soft skills via sessions including simulated patients and feedback from users.

These initiatives anticipate the reforms to graduate medical training due to be introduced in 2021 and which highlight the importance of internships and patient-doctor relations.

• Since 2019, simulations with feedback from users have also been used to train interns in how to present bad news. These sessions are run in parallel with "student MDT meetings", which put interns into the types of situations they are likely to encounter in real MDT meetings.

• Occitanie Regional Health Agency has awarded these courses its "Users' Rights" label in recognition of the way they have integrated simulated patients.

• Finally, a new approach to supervised evaluation was introduced in 2019 for the 140 medical students doing internships at the IUCT-Oncopole: an instructor watches the intern during a simulated interaction with a patient and then provides detailed feedback aimed at helping the intern improve his or her practices.

Experts in pediatric oncology

Prof. A. Laprie and Dr M. Pasquet are members of the advisory board for the National Diploma in Pediatric Oncology and the Specialist Transversal Training Program in Pediatric Oncology. Prof. A. Laprie also provides teaching in radiotherapy for pediatric cancers for the International Atomic Energy Agency (IAEA).

University diploma in cancer supportive care: Coordinated by Prof. F. Nourashemi, Dr N. Caunes-Hilary and Dr N. Saffon, the program is aimed at all medical and paramedical professionals.

New inter-university diploma in "Breast Oncology: from physiology to after cancer"

This new inter-university diploma was created in 2018 by Professors F. Trémollières, F. Dalenc and W. Jacot. Set up by the Universities of Toulouse and Montpellier and taught by healthcare professionals from Toulouse, Montpellier and Nimes, it involves lectures, practical courses and e-learning sessions. Fifteen students enrolled for the first year of the program, which began in February 2019 at the IUCT-Oncopole.

This course complements the eight existing university and inter-university diplomas associated with the IUCT-Oncopole.

Creation of a Journal Club

A weekly Journal Club was set up in November 2019 at the initiative of the "PhD Excellence" doctoral students' committee (COMET). Every week, a doctoral student presents a scientific paper to the rest of the IUCT-Oncopole's medical and scientific community.

Continuing training for healthcare professionals

• The IUCT-Oncopole organizes several seminar cycles for researchers and clinicians in the Toulouse area, the Occitanie region and throughout France.

• It also hosts the regional information and training meetings organized by the Onco-Occitanie network.

• Healthcare professionals and researchers are regularly invited to visit the IUCT-Oncopole's departments and facilities (pharmacy, radiotherapy department, etc.).

Forum on online-monitoring for cancer patients

Medical and paramedical professionals came to together on June 17, 2019, to discuss current research into online monitoring systems for cancer patients. The second part of the evening was used to present the IUCT-Oncopole's own initiatives.

Certified continuing training programs

• Since 2017, the IUCT-Oncopole, via the Institut Claudius Regaud, has been accredited by the European Society of Gynaecological Oncology (ESGO) to provide specialist training in gynecological oncology. Only seven other centers in France are certified to provide these two-year training courses. In 2019, Dr C. Gomez Roca became the first person to be awarded the "Diploma of European Gynaecological Oncologist" by the IUCT-Oncopole.

• The Institut Claudius Regaud's and GIPSE's training units run another 24 vocational training courses at the IUCT-Oncopole. Many of these programs use innovative tools, such as SPOCs. MYRE (MY Recordable E-learning) is an e-learning course that was developed by Dr L. Simon to enable radiation therapy technicians to continuously evaluate and expand their skills. In addition, steps are being taken to set up an e-learning platform for the IUCT-Oncopole. Baptized MyLittleTools, it will initially be available internally, before being made accessible to users outside the IUCT.

The first "Nutrition and Physical Education in Cancerology" training course

The first edition of the "Nutrition and Physical Education in Cancerology" training course took place on December 9, 2019. Designed and presented by members of the IUCT-Oncopole (M. Richl, Dr N. Caunes-Hilary and Dr N. Saadoune), this training course is a requirement for independent dieticians working within the ONCODIETS network, sponsored by the INTERCLAN of the Centers for the Fight Against Cancer. The program covers the impacts of undernutrition on cancer treatments and on the risks associated with excess weight and obesity, especially in terms of relapse.

Close collaboration with Oncostream

Oncostream is the French Society of Surgical Oncology's Web TV channel. Created in 2014 by L. Vaillat and Dr G. Ferron, it can be used to stream, either live or on demand, all types of oncology-related event and training course, ranging from the SFCO's annual conference to webinars on a wide variety of themes. 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 2019 including a trans-disciplinary discussion of sentinel lymph node surgery (with more than 1,500 live connections and more than 30,000 on-demand connections in the first month) and a seminar on breast reconstruction and anaplastic lymphomas. By providing a library of commentated surgical videos, this new teaching tool represents a major evolution in the way oncology surgeons update their knowledge.

Creation of an Oncogeriatrics 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, whose members include the IUCT-Oncopole's Geriatric Oncology OCC. The course is free and open to all, although it is primarily aimed at people who care for older patients. The first session will open on March 6, 2020, and last six weeks. Learners who complete the full course, which will require about 2 hours' work a week, will obtain a certificate.
https://mooc-oncogeriatrie.the-mooc-agency.com/

Information on patient therapeutic education

• The IUCT-Oncopole, in conjunction with patients' associations, holds numerous events, such as Pink October, to inform patients about advances in research and innovative therapies and to raise patients' awareness of organizations and measures that are available to help them in their day-to-day lives, both during and after treatment. Moreover, since June 2019, the Supportive Care Department, in partnership with CARSAT, has held quarterly meetings to advise patients on obtaining social security benefits.
• In 2018, the Occitanie Regional Health Agency appointed the IUCT-Oncopole the "sponsor and guarantor of the Cancerology Transversal Therapeutic Education Unit (UTEP) for the Occitanie Region". The UTEP's two main objectives are to develop therapeutic patient education (TPE) in Occitanie and to finalize the creation of a platform for patients receiving oral chemotherapy, a project the IUCT-Oncopole first launched in 2015.
• Two new therapeutic patient education (TPE) programs were launched in 2019 to help patients receiving hematopoietic stem-cell transplants. The project, coordinated by Dr A. Huynh, comprises a pre-transplant program ("3, 2, 1... Prêt? Greffe!" – contact person: L. Mercier) and a post-transplant program ("Le MAG (MonAlloGreffe): A La Une !" – contact person: F. Carantois), both of which are aimed at patients over the age of 15. Their goal is to reduce anxiety and prevent complications by informing patients about the transplant process, helping them prepare for it, both physically and mentally, and teaching them the necessary self-care skills.

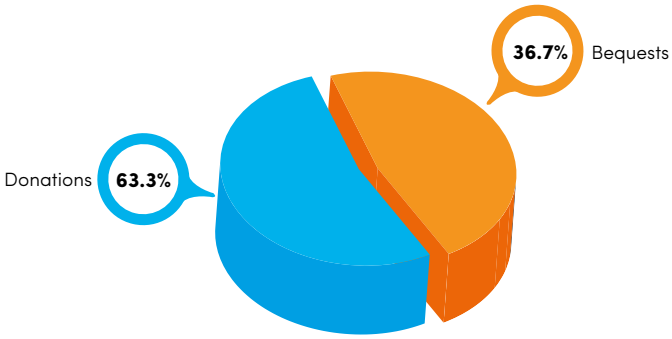
BRCA Cafés

"BRCA Café" is a discussion group for women with an hereditary predisposition to breast and ovarian cancer (carriers of BRCA-1, BRCA-2 and PALB2 genetic mutations) that meets every two months at "Les Fortes Têtes", a relaxed and friendly restaurant in the center of Toulouse. This novel initiative was launched in September 2018 by J. Grondin (Oncogenetics OCC) under the auspices of the GENEPY network. Twenty-one women attended BRCA Café meetings (max. 10 people per session) during the project's first year, with discussions centering mostly round the results of genetic tests, prophylactic surgery and explaining genetic information to family and friends.

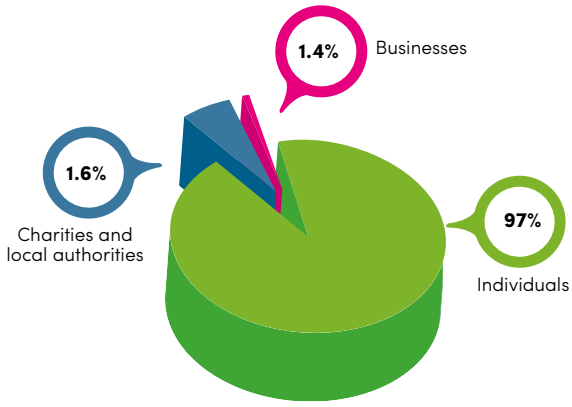
Support for our work

We would like to express our deepest gratitude to all those who supported us in 2019. Thanks to you – local authorities, businesses, charities, and, especially, private individuals – we are able to continue innovating and launching projects to identify and develop new therapeutic strategies that will improve the quality of life of our patients and their families.

We received **4,926 donations**, totaling **764,643 euros.**



Types of support



Types of support received in 2019

Almost four-fifths (79.71% = €512,541) of the donations and bequests received in 2019 were allocated directly to the IUCT-Oncopole's research activities (covering 4% of operating costs).

In 2019 the Fondation Toulouse Cancer Santé received 3,815 donations and bequests, amounting to €862,000 (62% from businesses, 38% from individuals).

Main publications in 2019

List of papers published in journals with an impact factor greater than 10
(papers whose first, second or penultimate author is a member of the IUCT-Oncopole are highlighted in orange).

1. André, F., Ciruelos, E., Rubovszky, G., Campone, M., Loibl, S., Rugo, H.S., Iwata, H., Conte, P., Mayer, I.A., Kaufman, B., Yamashita, T., Lu, Y.-S., Inoue, K., Takahashi, M., Pápai, Z., Longin, A.-S., Mills, D., Wilke, C., Hirawat, S., Juric, D., SOLAR-1 Study Group, the SOLAR-1 Study Group, 2019. **Alpelisib for PIK3CA-Mutated, Hormone Receptor-Positive Advanced Breast Cancer.** N. Engl. J. Med. 380, 1929–1940. https://doi.org/10.1056/NEJMoa1813904

2. Angenendt, L., Röllig, C., Montesinos, P., Martínez-Cuadrón, D., Barragan, E., García, R., Botella, C., Martínez, P., Ravandi, F., Kadia, T., Kantarjian, H.M., Cortes, J., Juliusson, G., Lazarevic, V., Höglund, M., Lehmann, S., Recher, C., Pigneux, A., Bertoli, S., Dumas, P.-Y., Dombret, H., Preudhomme, C., Micol, J.-B., Terré, C., Ráčil, Z., Novák, J., Žák, P., Wei, A.H., Tiong, I.S., Wall, M., Estey, E., Shaw, C., Exeler, R., Wagenführ, L., Stölzel, F., Thiede, C., Stelljes, M., Lenz, G., Mikesch, J.-H., Serve, H., Ehninger, G., Berdel, W.E., Kramer, M., Krug, U., Schliemann, C., 2019. **Chromosomal Abnormalities and Prognosis in NPM1-Mutated Acute Myeloid Leukemia: A Pooled Analysis of Individual Patient Data From Nine International Cohorts**. J. Clin. Oncol. JCO1900416. https://doi.org/10.1200/JCO.19.00416

3. Appay, R., Dehais, C., Maurage, C.-A., Alentorn, A., Carpentier, C., Colin, C., Ducray, F., Escande, F., Idbaih, A., Kamoun, A., Marie, Y., Mokhtari, K., Tabouret, E., Trabelsi, N., Uro-Coste, E., Delattre, J.-Y., Figarella-Branger, D., POLA Network, 2019. **CDKN2A homozygous deletion is a strong adverse prognosis factor in diffuse malignant IDH-mutant gliomas.** Neuro-oncology 21, 1519–1528. https://doi.org/10.1093/neuonc/noz124

4. Attal, M., Richardson, P.G., Rajkumar, S.V., San-Miguel, J., Beksac, M., Spicka, I., Leleu, X., Schjesvold, F., Moreau, P., Dimopoulos, M.A., Huang, J.S.-Y., Minarik, J., Cavo, M., Prince, H.M., Macé, S., Corzo, K.P., Campana, F., Le-Guennec, S., Dubin, F., Anderson, K.C., ICARIA-MM study group, 2019. **Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study.** Lancet. https://doi.org/10.1016/S0140-6736(19)32556-5

5. Bachelot, T., Ciruelos, E., Schneeweiss, A., Puglisi, F., Peretz-Yablonski, T., Bondarenko, I., Paluch-Shimon, S., Wardley, A., Merot, J.-L., du Toit, Y., Easton, V., Lindeggeer, N., Miles, D., PERUSE investigators, 2019. **Preliminary safety and efficacy of first-line pertuzumab combined with trastuzumab and taxane therapy for HER2-positive locally recurrent or metastatic breast cancer (PERUSE).** Ann. Oncol. 30, 766–773. https://doi.org/10.1093/annonc/mdz061

6. Bachy, E., Seymour, J.F., Feugier, P., Offner, F., López-Guillermo, A., Belada, D., Xerri, L., Catalano, J.V., Brice, P., Lemonnier, F., Martin, A., Casasnovas, O., Pedersen, L.M., Dorvaux, V., Simpson, D., Leppa, S., Gabarre, J., da Silva, M.G., Glaisner, S., Ysebaert, L., Vekhoff, A., Intragumtornchai, T., Le Gouill, S., Lister, A., Estell, J.A., Milone, G., Sonet, A., Farhi, J., Zeuner, H., Tilly, H., Salles, G., 2019. **Sustained Progression-Free Survival Benefit of Rituximab Maintenance in Patients with Follicular Lymphoma: Long-Term Results of the PRIMA Study**. J. Clin. Oncol. JCO1901073. https://doi.org/10.1200/JCO.19.01073

7. Basbous, J., Aze, A., Chaloin, L., Lebdy, R., Hodroj, D., Ribeyre, C., Larroque, M., Shepard, C., Kim, B., Pruvost, A., Moreaux, J., Maiorano, D., Mechali, M., Constantinou, A., 2019. **Dihydropyrimidinase protects from DNA replication stress caused by cytotoxic metabolites.** Nucleic Acids Res. https://doi.org/10.1093/nar/gkz1162

8. Ben Zouari, Y., Molitor, A.M., Sikorska, N., Pancaldi, V., Sexton, T., 2019. **ChiCMaxima: a robust and simple pipeline for detection and visualization of chromatin looping in Capture Hi-C.** Genome Biol. 20, 102. https://doi.org/10.1186/s13059-019-1706-3

9. Bertucci, F., Ng, C.K.Y., Patsouris, A., Droin, N., Piscuoglio, S., Carbuccia, N., Soria, J.C., Dien, A.T., Adnani, Y., Kamal, M., Garnier, S., Meurice, G., Jimenez, M., Dogan, S., Verret, B., Chaffanet, M., Bachelot, T., Campone, M., Lefeuvre, C., Bonnefoi, H., Dalenc, F., Jacquet, A., De Filippo, M.R., Babbar, N., Birnbaum, D., Filleron, T., Le Tourneau, C., André, F., 2019. **Genomic characterization of metastatic breast cancers.** Nature 569, 560–564. https://doi.org/10.1038/s41586-019-1056-z **Author** Correction: Genomic characterization of metastatic breast cancers. Nature. https://doi.org/10.1038/s41586-019-1380-3

10. Bianco, J.N., Bergoglio, V., Lin, Y.-L., Pillaire, M.-J., Schmitz, A.-L., Gilhodes, J., Lusque, A., Mazières, J., Lacroix-Triki, M., Roumeliotis, T.I., Choudhary, J., Moreaux, J., Hoffmann, J.-S., Tourrière, H., Pasero, P., 2019. **Overexpression of Claspin and Timeless protects cancer cells from replication stress in a checkpoint-independent manner**. Nat Commun 10, 910. https://doi.org/10.1038/s41467-019-08886-8

11. Blay, J.-Y., Honoré, C., Stoeckle, E., Meeus, P., Jafari, M., Gouin, F., Anract, P., Ferron, G., Rochwerger, A., Ropars, M., Carrere, S., Marchal, F., Sirveaux, F., Di Marco, A., Le Nail, L.R., Guiramand, J., Vaz, G., Machiavello, J.-C., Marco, O., Causeret, S., Gimbergues, P., Fiorenza, F., Chaigneau, L., Guillemin, F., Guilloit, J.-M., Dujardin, F., Spano, J.-P., Ruzic, J.-C., Michot, A., Soibinet, P., Bompas, E., Chevreau, C., Duffaud, F., Rios, M., Perrin, C., Firmin, N., Bertucci, F., Le Pechoux, C., Le Loarer, F., Collard, O., Karanian-Philippe, M., Brahmi, M., Dufresne, A., Dupré, A., Ducimetière, F., Giraud, A., Pérol, D., Toulmonde, M., Ray-Coquard, I., Italiano, A., Le Cesne, A., Penel, N., Bonvalot, S., NETSARC/REPPS/RESOS and French Sarcoma Group–Groupe d'Etude des Tumeurs Osseuses (GSF-GETO) Networks, 2019. **Surgery in reference centers improves survival of sarcoma patients: a nationwide study**. Ann. Oncol.

https://doi.org/10.1093/annonc/mdz124. Corrigendum in Ann. Oncol. 2019 DOI: 10.1093/annonc/mdz170

12. Bonvalot, S., Rutkowski, P.L., Thariat, J., Carrère, S., Ducassou, A., Sunyach, M.-P., Agoston, P., Hong, A., Mervoyer, A., Rastrelli, M., Moreno, V., Li, R.K., Tiangco, B., Herraez, A.C., Gronchi, A., Mangel, L., Sy-Ortin, T., Hohenberger, P., de Baère, T., Le Cesne, A., Helfre, S., Saada-Bouzid, E., Borkowska, A., Anghel, R., Co, A., Gebhart, M., Kantor, G., Montero, A., Loong, H.H., Vergés, R., Lapeire, L., Dema, S., Kacso, G., Austen, L., Moureau-Zabotto, L., Servois, V., Wardelmann, E., Terrier, P., Lazar, A.J., Bovée, J.V.M.G., Le Péchoux, C., Papai, Z., 2019. **NBTXR3, a first-in-class radioenhancer hafnium oxide nanoparticle, plus radiotherapy versus radiotherapy alone in patients with locally advanced soft-tissue sarcoma (Act.In.Sarc): a multicentre, phase 2-3, randomised, controlled trial.** Lancet Oncol. https://doi.org/10.1016/S1470-2045(19)30326-2

13. Bousquet Mur, E., Bernardo, S., Papon, L., Mancini, M., Fabbrizio, E., Goussard, M., Ferrer, I., Giry, A., Quantin, X., Pujol, J.-L., Calvayrac, O., Moll, H.P., Glasson, Y., Pirot, N., Turtoi, A., Cañamero, M., Wong, K.-K., Yarden, Y., Casanova, E., Soria, J.-C., Colinge, J., Siebel, C.W., Mazieres, J., Favre, G., Paz-Ares, L., Maraver, A., 2019. **Notch inhibition overcomes resistance to Tyrosine Kinase Inhibitors in EGFR-driven lung adenocarcinoma**. J. Clin. Invest. https://doi.org/10.1172/JCI126896

14. Camus, M., Hirschi, S., Prevot, G., Chenard, M.-P., Mal, H., Stern, M., Reynaud-Gaubert, M., Gilhodes, J., Burlet-Schiltz, O., Brousset, P., Colombat, M., 2019**. Proteomics evidence of specific IGKV1-8 association with cystic lung light chain deposition disease.** Blood. https://doi.org/10.1182/blood.2019898577

15. Cargnello, M., Topisirovic, I., 2019. **c-Myc steers translation in lymphoma**. J. Exp. Med. 216, 1471–1473. https://doi.org/10.1084/jem.20190721

16. Carrie, C., Magné, N., Burban-Provost, P., Sargos, P., Latorzeff, I., Lagrange, J.-L., Supiot, S., Belkacemi, Y., Peiffert, D., Allouache, N., Dubray, B.M., Servagi-Vernat, S., Suchaud, J.-P., Crehange, G., Guerif, S., Brihoum, M., Barbier, N., Graff-Cailleaud, P., Ruffion, A., Dussart, S., Ferlay, C., Chabaud, S., 2019. **Short-term androgen deprivation therapy combined with radiotherapy as salvage treatment after radical prostatectomy for prostate cancer (GETUG-AFU 16): a 112-month follow-up of a phase 3, randomised trial**. Lancet Oncol. https://doi.org/10.1016/S1470-2045(19)30486-3

17. Castinetti, F., Waguespack, S.G., Machens, A., Uchino, S., Lazaar, K., Sanso, G., Else, T., Dvorakova, S., Qi, X.P., Elisei, R., Maia, A.L., Glod, J., Lourenço, D.M., Valdes, N., Mathiesen, J., Wohllk, N., Bandgar, T.R., Drui, D., Korbonits, M., Druce, M.R., Brain, C., Kurzawinski, T., Patocs, A., Bugalho, M.J., Lacroix, A., Caron, P., Fainstein-Day, P., Borson Chazot, F., Klein, M., Links, T.P., Letizia, C., Fugazzola, L., Chabre, O., Canu, L., Cohen, R., Tabarin, A., Spehar Uroic, A., Maiter, D., Laboureau, S., Mian, C., Peczkowska, M., Sebag, F., Brue, T., Mirebeau-Prunier, D., Leclerc, L., Bausch, B., Berdelou, A., Sukurai, A., Vlcek, P., Krajewska, J., Barontini, M., Vaz Ferreira Vargas, C., Valerio, L., Ceolin, L., Akshintala, S., Hoff, A., Godballe, C., Jarzab, B., Jimenez, C., Eng, C., Imai, T., Schlumberger, M., Grubbs, E., Dralle, H., Neumann, H.P., Baudin, E., 2019. **Natural history, treatment, and long-term follow up of patients with multiple endocrine neoplasia type 2B: an international, multicentre, retrospective study.** Lancet Diabetes Endocrinol. https://doi.org/10.1016/S2213-8587(18)30336-X . Erratum in Lancet Diabetes Endocrinol. 2019. DOI: 10.1016/S2213-8587(19)30037-3

18. Roos-Weil, D., Dillard, C., Gabillaud, C., Maloum, K., Settegrana, C., Baseggio, L., Lesesve, J.-F., Yon, M., Jondreville, L., Lesty, C., Davi, F.B., Le Garff-Tavernier, M., Droin, N.M., Dessen, P., Algrin, C., Leblond, V., Gabarre, J., Bouzy, S., Eclache, V., Gaillard, B., Callet-Bauchu, E., Muller, M., Lefebvre, C., Nadal, N., Ittel, A., Struski, S., Collonge-Rame, M.-A., Quilichini, B., Fert-Ferrer, S., Auger, N., Radford-Weiss, I., Wagner, L., Scheinost, S., Zenz, T., Susin, S.A., Bernard, O.A., Nguyen-Khac, F., 2019**. Genetic characterization of B-cell prolymphocytic leukemia: a prognostic model involving MYC and TP53.** Blood. https://doi.org/10.1182/blood.2019001187

19. Cheminant, M., Mahlaoui, N., Desconclois, C., Canioni, D., Ysebaert, L., Dupré, L., Vasconcelos, Z., Malphettes, M., Moshous, D., Neven, B., Rohrlich, P.-S., Bernard, M., Bertrand, Y., Fischer, A., Suarez, F., 2019. **Lymphoproliferative Disease in Wiskott-Aldrich Syndrome. Analysis of the French Registry of Primary Immunodeficiencies**. J. Allergy Clin. Immunol. https://doi.org/10.1016/j.jaci.2019.01.046

20. Chung, H.C., Piha-Paul, S.A., Lopez-Martin, J., Schellens, J.H.M., Kao, S., Miller, W.H., Delord, J.-P., Gao, B., Planchard, D., Gottfried, M., Zer, A., Jalal, S.I., Penel, N., Mehnert, J.M., Matos, I., Bennouna, J., Kim, D.-W., Xu, L., Krishnan, S., Norwood, K., Ott, P.A., 2019. **Pembrolizumab After Two or More Lines of Previous Therapy in Patients With Recurrent or Metastatic Small-Cell Lung Cancer: Results From the KEYNOTE-028 and KEYNOTE-158 Studies.** J Thorac Oncol. https://doi.org/10.1016/j.jtho.2019.12.109

21. Chung, H.C., Ros, W., Delord, J.-P., Perets, R., Italiano, A., Shapira-Frommer, R., Manzuk, L., Piha-Paul, S.A., Xu, L., Zeigenfuss, S., Pruitt, S.K., Leary, A., 2019. **Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study**. J. Clin. Oncol. JCO1801265. https://doi.org/10.1200/JCO.18.01265

22. Cohen, E.E.W., Soulières, D., Le Tourneau, C., Dinis, J., Licitra, L., Ahn, M.-J., Soria, A., Machiels, J.-P., Mach, N., Mehra, R., Burtness, B., Zhang, P., Cheng, J., Swaby, R.F., Harrington, K.J., KEYNOTE-040 investigators, 2019. **Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised,**

open-label, phase 3 study. Lancet 393, 156–167. https://doi.org/10.1016/S0140-6736(18)31999-8

23. Curdy, N., Lanvin, O., Laurent, C., Fournié, J.-J., Franchini, D.-M., 2019. **Regulatory Mechanisms of Inhibitory Immune Checkpoint Receptors Expression.** Trends Cell Biol. https://doi.org/10.1016/j.tcb.2019.07.002

24. Delanoy, N., Michot, J.-M., Comont, T., Kramkimel, N., Lazarovici, J., Dupont, R., Champiat, S., Chahine, C., Robert, C., Herbaux, C., Besse, B., Guillemin, A., Mateus, C., Pautier, P., Saïag, P., Madonna, E., Maerevoet, M., Bout, J.-C., Leduc, C., Biscay, P., Quere, G., Nardin, C., Ebbo, M., Albigès, L., Marret, G., Levrat, V., Dujon, C., Vargaftig, J., Laghouati, S., Croisille, L., Voisin, A.-L., Godeau, B., Massard, C., Ribrag, V., Marabelle, A., Michel, M., Lambotte, O., 2019. **Haematological immune-related adverse events induced by anti-PD-1 or anti-PD-L1 immunotherapy: a descriptive observational study.** Lancet Haematol 6, e48–e57. https://doi.org/10.1016/S2352-3026(18)30175-3

25. Emens, L.A., Cruz, C., Eder, J.P., Braiteh, F., Chung, C., Tolaney, S.M., Kuter, I., Nanda, R., Cassier, P.A., Delord, J.-P., Gordon, M.S., ElGabry, E., Chang, C.-W., Sarkar, I., Grossman, W., O'Hear, C., Fassò, M., Molinero, L., Schmid, P., 2019. **Long-term Clinical Outcomes and Biomarker Analyses of Atezolizumab Therapy for Patients With Metastatic Triple-Negative Breast Cancer: A Phase 1 Study**. JAMA Oncol 5, 74–82. https://doi.org/10.1001/jamaoncol.2018.4224

26. Facon, T., Kumar, S., Plesner, T., Orlowski, R.Z., Moreau, P., Bahlis, N., Basu, S., Nahi, H., Hulin, C., Quach, H., Goldschmidt, H., O'Dwyer, M., Perrot, A., Venner, C.P., Weisel, K., Mace, J.R., Raje, N., Attal, M., Tiab, M., Macro, M., Frenzel, L., Leleu, X., Ahmadi, T., Chiu, C., Wang, J., Van Rampelbergh, R., Uhlar, C.M., Kobos, R., Qi, M., Usmani, S.Z., MAIA Trial Investigators, 2019. **Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma.** N. Engl. J. Med. 380, 2104–2115. https://doi.org/10.1056/NEJMoa1817249

27. Farge, D., Frere, C., Connors, J.M., Ay, C., Khorana, A.A., Munoz, A., Brenner, B., Kakkar, A., Rafii, H., Solymoss, S., Brilhante, D., Monreal, M., Bounameaux, H., Pabinger, I., Douketis, J., International Initiative on Thrombosis and Cancer (ITAC) advisory panel, 2019. **2019 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer.** Lancet Oncol. 20, e566–e581. https://doi.org/10.1016/S1470-2045(19)30336-5

28.Ferreira, A.R., Di Meglio, A., Pistilli, B., Gbenou, A.S., El-Mouhebb, M., Dauchy, S., Charles, C., Joly, F., Everhard, S., Lambertini, M., Coutant, C., Cottu, P., Lerebours, F., Petit, T., Dalenc, F., Rouanet, P., Arnaud, A., Martin, A., Berille, J., Ganz, P.A., Partridge, A.H., Delaloge, S., Michiels, S., Andre, F., Vaz-Luis, I., 2019. **Differential impact of endocrine therapy and chemotherapy on quality of life of breast cancer survivors: a prospective patient-reported outcomes analysis.** Ann. Oncol. https://doi.org/10.1093/annonc/mdz298

29. Flinn, I.W., Gribben, J.G., Dyer, M.J.S., Wierda, W., Maris, M.B., Furman, R.R., Hillmen, P., Rogers, K.A., Padmanabhan Iyer, S., Quillet-Mary, A., Ysebaert, L., Walter, H.S., Verdugo, M., Klein, C., Huang, H., Jiang, Y., Lozanski, G., Pignataro, D.S., Humphrey, K., Mobasher, M., Kipps, T.J., 2019. **Phase 1b study of venetoclax-obinutuzumab in previously untreated and relapsed/refractory chronic lymphocytic leukemia**. Blood. https://doi.org/10.1182/blood-2019-01-896290

30. Flippot, R., Dalban, C., Laguerre, B., Borchiellini, D., Gravis, G., Négrier, S., Chevreau, C., Joly, F., Geoffrois, L., Ladoire, S., Mahammedi, H., Rolland, F., Gross-Goupil, M., Deluche, E., Priou, F., Laramas, M., Barthélémy, P., Narciso, B., Houedé, N., Culine, S., Oudard, S., Chenot, M., Tantot, F., Chabaud, S., Escudier, B., Albiges, L., 2019. **Safety and Efficacy of Nivolumab in Brain Metastases From Renal Cell Carcinoma: Results of the GETUG-AFU 26 NIVOREN Multicenter Phase II Study.** J. Clin. Oncol. JCO1802218. https://doi.org/10.1200/JCO.18.02218

31. Frere, C., Bournet, B., Gourgou, S., Fraisse, J., Canivet, C., Connors, J.M., Buscail, L., Farge, D., BACAP Consortium, 2019. **Incidence of Venous Thromboembolism in Patients with Newly Diagnosed Pancreatic Cancer and Factors Associated With Outcomes**. Gastroenterology. https://doi.org/10.1053/j.gastro.2019.12.009

32. Goehrig, D., Nigri, J., Samain, R., Wu, Z., Cappello, P., Gabiane, G., Zhang, X., Zhao, Y., Kim, I.-S., Chanal, M., Curto, R., Hervieu, V., de La Fouchardière, C., Novelli, F., Milani, P., Tomasini, R., Bousquet, C., Bertolino, P., Hennino, A., 2019. **Stromal protein βig-h3 reprogrammes tumour microenvironment in pancreatic cancer**. Gut 68, 693–707. https://doi.org/10.1136/gutjnl-2018-317570

33. Gomez-Roca, C.A., Italiano, A., Le Tourneau, C., Cassier, P.A., Toulmonde, M., D'Angelo, S.P., Campone, M., Weber, K.L., Loirat, D., Cannarile, M.A., Jegg, A.-M., Ries, C., Christen, R., Meneses-Lorente, G., Jacob, W., Klaman, I., Ooi, C.-H., Watson, C., Wonde, K., Reis, B., Michielin, F., Rüttinger, D., Delord, J.-P., Blay, J.-Y., 2019. **Phase I Study of Emactuzumab Single Agent or in Combination with Paclitaxel in Patients with Advanced/Metastatic Solid Tumors Reveals Depletion of Immunosuppressive M2-like Macrophages.** Ann. Oncol. https://doi.org/10.1093/annonc/mdz163

34.González Besteiro, M.A., Calzetta, N.L., Loureiro, S.M., Habif, M., Bétous, R., Pillaire, M.-J., Maffia, A., Sabbioneda, S., Hoffmann, J.-S., Gottifredi, V., 2019. **Chk1 loss creates replication barriers that compromise cell survival independently of excess origin firing.** EMBO J. e101284. https://doi.org/10.15252/embj.2018101284

35. Hadjadj, J., Aladjidi, N., Fernandes, H., Leverger, G., Magérus-Chatinet, A., Mazerolles, F., Stolzenberg, M.-C.,

Jacques, S., Picard, C., Rosain, J., Fourrage, C., Hanein, S., Zarhrate, M., Pasquet, M., Abou Chahla, W., Barlogis, V., Bertrand, Y., Pellier, I., Colomb Bottollier, E., Fouyssac, F., Blouin, P., Thomas, C., Cheikh, N., Dore, E., Pondarre, C., Plantaz, D., Jeziorski, E., Millot, F., Garcelon, N., Ducassou, S., Perel, Y., Leblanc, T., Neven, B., Fischer, A., Rieux-Laucat, F., members of the French Reference Center for Pediatric Autoimmune Cytopenia (CEREVANCE), 2019. **Pediatric Evans syndrome is associated with a high frequency of potentially damaging variants in immune genes**. Blood 134, 9–21. https://doi.org/10.1182/blood-2018-11-887141

36. Hassan, R., Thomas, A., Nemunaitis, J.J., Patel, M.R., Bennouna, J., Chen, F.L., Delord, J.-P., Dowlati, A., Kochuparambil, S.T., Taylor, M.H., Powderly, J.D., Vaishampayan, U.N., Verschraegen, C., Grote, H.J., von Heydebreck, A., Chin, K., Gulley, J.L., 2019. **Efficacy and Safety of Avelumab Treatment in Patients With Advanced Unresectable Mesothelioma: Phase 1b Results From the JAVELIN Solid Tumor Trial**. JAMA Oncol. https://doi.org/10.1001/jamaoncol.2018.5428

37. Heinhuis, K.M., Carlino, M., Joerger, M., Di Nicola, M., Meniawy, T., Rottey, S., Moreno, V., Gazzah, A., Delord, J.-P., Paz-Ares, L., Britschgi, C., Schilder, R.J., O'Byrne, K., Curigliano, G., Romano, E., Patah, P., Wang, R., Liu, Y., Bajaj, G., Siu, L.L., 2019. **Safety, Tolerability, and Potential Clinical Activity of a Glucocorticoid-Induced TNF Receptor-Related Protein Agonist Alone or in Combination With Nivolumab for Patients With Advanced Solid Tumors: A Phase 1/2a Dose-Escalation and Cohort-Expansion Clinical Trial.** JAMA Oncol 1–8. https://doi.org/10.1001/jamaoncol.2019.3848

38. Hendriks, L.E.L., Henon, C., Auclin, E., Mezquita, L., Ferrara, R., Audigier-Valette, C., Mazieres, J., Lefebvre, C., Rabeau, A., Le Moulec, S., Cousin, S., Duchemann, B., le Pechoux, C., Botticella, A., Ammari, S., Gazzah, A., Caramella, C., Adam, J., Lechapt, E., Planchard, D., de Ruysscher, D., Dingemans, A.-M., Besse, B., 2019. **Outcome of patients with non-small cell lung cancer and brain metastases treated with checkpoint inhibitors**. J Thorac Oncol. https://doi.org/10.1016/j.jtho.2019.02.009

39. Herms, F., Lambert, J., Grob, J.-J., Haudebourg, L., Bagot, M., Dalac, S., Dutriaux, C., Guillot, B., Jeudy, G., Mateus, C., Monestier, S., Mortier, L., Poulalhon, N., Prey, S., Robert, C., Vabres, P., Lebbe, C., Meyer, N., Basset-Seguin, N., 2019. **Follow-Up of Patients With Complete Remission of Locally Advanced Basal Cell Carcinoma After Vismodegib Discontinuation: A Multicenter French Study of 116 Patients**. J. Clin. Oncol. JCO1800794. https://doi.org/10.1200/JCO.18.00794

40. Hoeben, B.A., Carrie, C., Timmermann, B., Mandeville, H.C., Gandola, L., Dieckmann, K., Ramos Albiac, M., Magelssen, H., Lassen-Ramshad, Y., Ondrová, B., Ajithkumar, T., Alapetite, C., Balgobind, B.V., Bolle, S., Cameron, A.L., Davila Fajardo, R., Dietzsch, S., Dumont Lecomte, D., van den Heuvel-Eibrink, M.M., Kortmann, R.D., Laprie, A., Melchior, P., Padovani, L., Rombi, B., Scarzello, G., Schwarz, R., Seiersen, K., Seravalli, E., Thorp, N., Whitfield, G.A., Boterberg, T., Janssens, G.O., 2019. **Management of vertebral radiotherapy dose in paediatric patients with cancer: consensus recommendations from the SIOPE radiotherapy working group**. Lancet Oncol. 20, e155–e166. https://doi.org/10.1016/S1470-2045(19)30034-8

41. Hofman, V., Rouquette, I., Long-Mira, E., Piton, N., Chamorey, E., Heeke, S., Vignaud, J.M., Yguel, C., Mazières, J., Lepage, A.-L., Bibeau, F., Begueret, H., Lassalle, S., Lalvée, S., Zahaf, K., Benzaquen, J., Poudenx, M., Marquette, C.-H., Sabourin, J.-C., Ilié, M., Hofman, P., 2019. **Multicenter evaluation of a novel ROS1 immunohistochemistry assay (SP384) for detection of ROS1 rearrangements in a large cohort of lung adenocarcinoma patients**. J Thorac Oncol. https://doi.org/10.1016/j.jtho.2019.03.024

42. Jeanson, A., Tomasini, P., Souquet-Bressand, M., Brandone, N., Boucekine, M., Grangeon, M., Chaleat, S., Khobta, N., Milia, J., Mhanna, L., Greillier, L., Biemar, J., Nanni, I., Ouafik, L., Garcia, S., Mazières, J., Barlesi, F., Mascaux, C., 2019. **Brief report: efficacy of immune checkpoint inhibitors in KRAS-mutant Non-small cell lung cancer (NSCLC)**. J Thorac Oncol. https://doi.org/10.1016/j.jtho.2019.01.011

43. Kaboré, E.G., Guenancia, C., Vaz-Luis, I., Di Meglio, A., Pistilli, B., Coutant, C., Cottu, P., Lesur, A., Petit, T., Dalenc, F., Rouanet, P., Arnaud, A., Arsene, O., Ibrahim, M., Wassermann, J., Boileau-Jolimoy, G., Martin, A.-L., Lemonnier, J., André, F., Arveux, P., 2019. **Association of body mass index and cardiotoxicity related to anthracyclines and trastuzumab in early breast cancer: French CANTO cohort study.** PLoS Med. 16, e1002989. https://doi.org/10.1371/journal.pmed.1002989

44. Labreche, K., Daniau, M., Sud, A., Law, P.J., Royer-Perron, L., Holroyd, A., Broderick, P., Went, M., Benazra, M., Ahle, G., Soubeyran, P., Taillandier, L., Chinot, O.L., Casasnovas, O., Bay, J.-O., Jardin, F., Oberic, L., Fabbro, M., Damaj, G., Brion, A., Mokhtari, K., Philippe, C., Sanson, M., Houillier, C., Soussain, C., Hoang-Xuan, K., Houlston, R.S., Alentorn, A., LOC Network, 2019. **A genome-wide association study identifies susceptibility loci for primary central nervous system lymphoma at 6p25.3 and 3p22.1: a LOC network study**. Neuro-oncology. https://doi.org/10.1093/neuonc/noz088

45. Lambo, S., Gröbner, S.N., Rausch, T., Waszak, S.M., Schmidt, C., Gorthi, A., Romero, J.C., Mauermann, M., Brabetz, S., Krausert, S., Buchhalter, I., Koster, J., Zwijnenburg, D.A., Sill, M., Hübner, J.-M., Mack, N., Schwalm, B., Ryzhova, M., Hovestadt, V., Papillon-Cavanagh, S., Chan, J.A., Landgraf, P., Ho, B., Milde, T., Witt, O., Ecker, J., Sahm, F., Sumerauer, D., Ellison, D.W., Orr, B.A., Darabi, A., Haberler, C., Figarella-Branger, D., Wesseling, P., Schittenhelm, J., Remke, M., Taylor, M.D., Gil-da-Costa, M.J., Łastowska, M., Grajkowska, W., Hasselblatt, M., Hauser, P., Pietsch, T., Uro-Coste, E., Bourdeaut, F., Masliah-Planchon, J., Rigau, V., Alexandrescu, S., Wolf, S., Li, X.-N., Schüller,

U., Snuderl, M., Karajannis, M.A., Giangaspero, F., Jabado, N., von Deimling, A., Jones, D.T.W., Korbel, J.O., von Hoff, K., Lichter, P., Huang, A., Bishop, A.J.R., Pfister, S.M., Korshunov, A., Kool, M., 2019. **The molecular landscape of ETMR at diagnosis and relapse.** Nature. https://doi.org/10.1038/s41586-019-1815-x

46. Laurent, C., Nicolae, A., Laurent, C., Le Bras, F., Haioun, C., Fataccioli, V., Amara, N., Adélaïde, J., Guille, A., Schiano, J.-M., Tesson, B., Traverse-Glehen, A., Chenard, M.-P., Mescam, L., Moreau, A., Chassagne-Clement, C., Somja, J., Escudié, F., André, M., Martin, N., Lacroix, L., Lemonnier, F., Hamy-Petit, A.-S., Reyal, F., Bannier, M., Oberic, L., Prade, N., Frénois, F.-X., Beldi-Ferchiou, A., Delfau-Larue, M.-H., Bouabdallah, R., Birnbaum, D., Brousset, P., Xerri, L., Gaulard, P., 2019. **Gene alterations in epigenetic modifiers and JAK-STAT signaling are frequent in breast implant-associated ALCL.** Blood. https://doi.org/10.1182/blood.2019001904

47. Le, D.T., Kim, T.W., Van Cutsem, E., Geva, R., Jäger, D., Hara, H., Burge, M., O'Neil, B., Kavan, P., Yoshino, T., Guimbaud, R., Taniguchi, H., Elez, E., Al-Batran, S.-E., Boland, P.M., Crocenzi, T., Atreya, C.E., Cui, Y., Dai, T., Marinello, P., Diaz, L.A., André, T., 2019. **Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability-High/Mismatch Repair-Deficient Metastatic Colorectal Cancer: KEYNOTE-164.** J. Clin. Oncol. JCO1902107. https://doi.org/10.1200/JCO.19.02107

48. Lebbé, C., Meyer, N., Mortier, L., Marquez-Rodas, I., Robert, C., Rutkowski, P., Menzies, A.M., Eigentler, T., Ascierto, P.A., Smylie, M., Schadendorf, D., Ajaz, M., Svane, I.M., Gonzalez, R., Rollin, L., Lord-Bessen, J., Saci, A., Grigoryeva, E., Pigozzo, J., 2019. **Evaluation of Two Dosing Regimens for Nivolumab in Combination With Ipilimumab in Patients With Advanced Melanoma: Results From the Phase IIIb/IV CheckMate 511 Trial.** J. Clin. Oncol. JCO1801998. https://doi.org/10.1200/JCO.18.01998

49. Legros, L., Nicolini, F.E., Etienne, G., Rousselot, P., Rea, D., Giraudier, S., Guerci, A., Huguet, F., Gardembas, M., Ianotto, J.-C., Escoffre-Barbe, M., Coiteux, V., Varet, B., Morisset, S., Mahon, F.-X., 2019. **The TKI-Free Duration after a First Discontinuation Attempt That Failed in CP CML Patients Is a Predictive Factor of TKI-Free Remission after a Second Attempt**. Blood 134, 28. https://doi.org/10.1182/blood-2019-123719

50. Lopez, C.K., Noguera, E., Stavropoulou, V., Robert, E., Aid, Z., Ballerini, P., Bilhou-Nabera, C., Lapillonne, H., Boudia, F., Thirant, C., Fagnan, A., Arcangeli, M.-L., Kinston, S.J., Diop, M., Job, B., Lecluse, Y., Brunet, E., Babin, L., Villeval, J.L., Delabesse, E., Peters, A.H.F.M., Vainchenker, W., Gaudry, M., Masetti, R., Locatelli, F., Malinge, S., Nerlov, C., Droin, N., Lobry, C., Godin, I., Bernard, O.A., Gottgens, B., Petit, A., Pflumio, F., Schwaller, J., Mercher, T., 2019. **Ontogenic changes in hematopoietic hierarchy determine pediatric specificity and disease phenotype in fusion oncogene-driven myeloid leukemia**. Cancer Discov. https://doi.org/10.1158/2159-8290.CD-18-1463

51. Ludmir, E.B., Mahajan, A., Ahern, V., Ajithkumar, T., Alapetite, C., Bernier-Chastagner, V., Bindra, R.S., Bishop, A.J., Bolle, S., Brown, P.D., Carrie, C., Chalmers, A.J., Chang, E.L., Chung, C., Dieckmann, K., Esiashvili, N., Gandola, L., Ghia, A.J., Gondi, V., Grosshans, D.R., Harrabi, S.B., Horan, G., Indelicato, D.J., Jalali, R., Janssens, G.O., Krause, M., Laack, N.N., Laperriere, N., Laprie, A., Li, J., Marcus, K.J., McGovern, S.L., Merchant, T.E., Merrell, K.W., Padovani, L., Parkes, J., Paulino, A.C., Schwarz, R., Shih, H.A., Souhami, L., Sulman, E.P., Taylor, R.E., Thorp, N., Timmermann, B., Wheeler, G., Wolden, S.L., Woodhouse, K.D., Yeboa, D.N., Yock, T.I., Kortmann, R.-D., McAleer, M.F., 2019. **Assembling the brain trust: the multidisciplinary imperative in neuro-oncology**. Nat Rev Clin Oncol. https://doi.org/10.1038/s41571-019-0235-z

52. Mahlaoui, N., Picard, C., Bach, P., Costes, L., Courteille, V., Ranohavimparany, A., Alcaïs, A., Jais, J.-P., Fischer, A., CEREDIH French PID study group, 2019. **Genetic diagnosis of primary immunodeficiencies: A survey of the French national registry.** J. Allergy Clin. Immunol. 143, 1646–1649. e10. https://doi.org/10.1016/j.jaci.2018.12.994

53. Mansouri, I., Allodji, R.S., Hill, C., El-Fayech, C., Pein, F., Diallo, S., Schwartz, B., Vu-Bezin, G., Veres, C., Souchard, V., Dumas, A., Bolle, S., Thomas-Teinturier, C., Pacquement, H., Munzer, M., Bondiau, P.-Y., Berchery, D., Fresneau, B., Oberlin, O., Diallo, I., De Vathaire, F., Haddy, N., 2019. **The role of irradiated heart and left ventricular volumes in heart failure occurrence after childhood cancer**. Eur. J. Heart Fail. 21, 509–518. https://doi.org/10.1002/ejhf.1376 **If 13.965**

54. Marabelle, A., Le, D.T., Ascierto, P.A., Di Giacomo, A.M., De Jesus-Acosta, A., Delord, J.-P., Geva, R., Gottfried, M., Penel, N., Hansen, A.R., Piha-Paul, S.A., Doi, T., Gao, B., Chung, H.C., Lopez-Martin, J., Bang, Y.-J., Frommer, R.S., Shah, M., Ghori, R., Joe, A.K., Pruitt, S.K., Diaz, L.A., 2019. **Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study**. J. Clin. Oncol. JCO1902105. https://doi.org/10.1200/JCO.19.02105

55. Mariette, C., Markar, S.R., Dabakuyo-Yonli, T.S., Meunier, B., Pezet, D., Collet, D., D'Journo, X.B., Brigand, C., Perniceni, T., Carrère, N., Mabrut, J.-Y., Msika, S., Peschaud, F., Prudhomme, M., Bonnetain, F., Piessen, G., Fédération de Recherche en Chirurgie (FRENCH) and French Eso-Gastric Tumors (FREGAT) Working Group, 2019. **Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer.** N. Engl. J. Med. 380, 152–162. https://doi.org/10.1056/NEJMoa1805101

56. Marion, O., Lhomme, S., Nayrac, M., Dubois, M., Pucelle, M., Requena, M., Migueres, M., Abravanel, F., Peron, J.M.,

Carrere, N., Suc, B., Delobel, P., Kamar, N., Izopet, J., 2019. **Hepatitis E virus replication in human intestinal cells**. Gut. https://doi.org/10.1136/gutjnl-2019-319004

57. Maura, F., Bolli, N., Angelopoulos, N., Dawson, K.J., Leongamornlert, D., Martincorena, I., Mitchell, T.J., Fullam, A., Gonzalez, S., Szalat, R., Abascal, F., Rodriguez-Martin, B., Samur, M.K., Glodzik, D., Roncador, M., Fulciniti, M., Tai, Y.T., Minvielle, S., Magrangeas, F., Moreau, P., Corradini, P., Anderson, K.C., Tubio, J.M.C., Wedge, D.C., Gerstung, M., Avet-Loiseau, H., Munshi, N., Campbell, P.J., 2019. **Genomic landscape and chronological reconstruction of driver events in multiple myeloma.** Nat Commun 10, 3835. https://doi.org/10.1038/s41467-019-11680-1

58. Maura, F., Degasperi, A., Nadeu, F., Leongamornlert, D., Davies, H., Moore, L., Royo, R., Zicchedda, B., Puente, X.S., Avet-Loiseau, H., Cambell, P.J., Nik-Zainal, S., Campo, E., Munshi, N., Bolli, N., 2019. **A practical guide for mutational signature analysis in hematological malignancies**. Nat Commun 10, 2969. https://doi.org/10.1038/s41467-019-11037-8 Author Correction: in Nat Commun 10, 3431. https://doi.org/10.1038/s41467-019-11468-3

59. Mazières, J., Drilon, A., Lusque, A., Mhanna, L., Cortot, A.B., Mezquita, L., Thai, A.A., Mascaux, C., Couraud, S., Veillon, R., Van Den Heuvel, M., Neal, J., Peled, N., Früh, M., Ng, T.L., Gounant, V., Popat, S., Diebold, J., Sabari, J., Zhu, V.W., Rothschild, S.I., Bironzo, P., Martinez, A., Curioni-Fontecedro, A., Rosell, R., Lattuca-Truc, M., Wiesweg, M., Besse, B., Solomon, B., Barlesi, F., Schouten, R.D., Wakelee, H., Camidge, D.R., Zalcman, G., Novello, S., Ou, S.I., Milia, J., Gautschi, O., 2019. **Immune checkpoint inhibitors for patients with advanced lung cancer and oncogenic driver alterations: results from the IMMUNOTARGET registry**. Ann. Oncol. https://doi.org/10.1093/annonc/mdz167

60. Mazieres, J., Kowalski, D., Luft, A., Vicente, D., Tafreshi, A., Gümüş, M., Laktionov, K., Hermes, B., Cicin, I., Rodríguez-Cid, J., Wilson, J., Kato, T., Ramlau, R., Novello, S., Reddy, S., Kopp, H.-G., Piperdi, B., Li, X., Burke, T., Paz-Ares, L., 2019. **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**. J. Clin. Oncol. JCO1901348. https://doi.org/10.1200/JCO.19.01348

61. Michallet, A.-S., Dilhuydy, M.-S., Subtil, F., Rouille, V., Mahe, B., Laribi, K., Villemagne, B., Salles, G., Tournilhac, O., Delmer, A., Portois, C., Pegourie, B., Leblond, V., Tomowiak, C., de Guibert, S., Orsini, F., Banos, A., Carassou, P., Cartron, G., Fornecker, L.M., Ysebaert, L., Dartigeas, C., Truchan Graczyk, M., Vilque, J.P., Aurran, T., Cymbalista, F., Lepretre, S., Lévy, V., Nguyen-Khac, F., Le Garff-Tavernier, M., Aanei, C., Ticchioni, M., Letestu, R., Feugier, P., 2019. **Obinutuzumab and ibrutinib induction therapy followed by a minimal residual disease-driven strategy in patients with chronic lymphocytic leukaemia (ICLL07 FILO): a single-arm, multicentre, phase 2 trial.** Lancet Haematol. https://doi.org/10.1016/S2352-3026(19)30113-9

62. Mondragón, L., Mhaidly, R., De Donatis, G.M., Tosolini, M., Dao, P., Martin, A.R., Pons, C., Chiche, J., Jacquin, M., Imbert, V., Proïcs, E., Boyer, L., Doye, A., Luciano, F., Neels, J.G., Coutant, F., Fabien, N., Sormani, L., Rubio-Patiño, C., Bossowski, J.P., Muller, F., Marchetti, S., Villa, E., Peyron, J.-F., Gaulard, P., Lemonnier, F., Asnafi, V., Genestier, L., Benhida, R., Fournié, J.-J., Passeron, T., Ricci, J.-E., Verhoeyen, E., 2019. **GAPDH Overexpression in the T Cell Lineage Promotes Angioimmunoblastic T Cell Lymphoma through an NF-κB-Dependent Mechanism.** Cancer Cell. https://doi.org/10.1016/j.ccell.2019.07.008

63. Moreau, P., Attal, M., Hulin, C., Arnulf, B., Belhadj, K., Benboubker, L., Béné, M.C., Broijl, A., Caillon, H., Caillot, D., Corre, J., Delforge, M., Dejoie, T., Doyen, C., Facon, T., Sonntag, C., Fontan, J., Garderet, L., Jie, K.-S., Karlin, L., Kuhnowski, F., Lambert, J., Leleu, X., Lenain, P., Macro, M., Mathiot, C., Orsini-Piocelle, F., Perrot, A., Stoppa, A.-M., van de Donk, N.W., Wuilleme, S., Zweegman, S., Kolb, B., Touzeau, C., Roussel, M., Tiab, M., Marolleau, J.-P., Meuleman, N., Vekemans, M.-C., Westerman, M., Klein, S.K., Levin, M.-D., Fermand, J.P., Escoffre-Barbe, M., Eveillard, J.-R., Garidi, R., Ahmadi, T., Zhuang, S., Chiu, C., Pei, L., de Boer, C., Smith, E., Deraedt, W., Kampfenkel, T., Schecter, J., Vermeulen, J., Avet-Loiseau, H., Sonneveld, P., 2019. **Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study.** Lancet. https://doi.org/10.1016/S0140-6736(19)31240-1

64. Moro-Sibilot, D., Cozic, N., Pérol, M., Mazières, J., Otto, J., Souquet, P.J., Bahleda, R., Wislez, M., Zalcman, G., De Guibert, S., Barlési, F., Mennecier, B., Monnet, I., Sabatier, R., Bota, S., Dubos, C., Verriele, V., Haddad, V., Ferretti, G., Cortot, A., De Fraipont, F., Jimenez, M., Hoog-Labouret, N., Vassal, G., 2019. **Crizotinib in c-MET- or ROS1-positive NSCLC: results of the AcSé phase II trial**. Ann. Oncol. https://doi.org/10.1093/annonc/mdz407

65. Motta, J.-P., Denadai-Souza, A., Sagnat, D., Guiraud, L., Edir, A., Bonnart, C., Sebbag, M., Rousset, P., Lapeyre, A., Seguy, C., Mathurine-Thomas, N., Galipeau, H.J., Bonnet, D., Alric, L., Buret, A.G., Wallace, J.L., Dufour, A., Verdu, E.F., Hollenberg, M.D., Oswald, E., Serino, M., Deraison, C., Vergnolle, N., 2019**. Active thrombin produced by the intestinal epithelium controls mucosal biofilms.** Nat Commun 10, 3224. https://doi.org/10.1038/s41467-019-11140-w

66. Munshi, N.C., Jagannath, S., Avet-Loiseau, H., 2019. **Monoclonal Gammopathy May Be of Unpredictable Significance**. JAMA Oncol. https://doi.org/10.1001/jamaoncol.2019.1580

67. Naumann, R.W., Hollebecque, A., Meyer, T., Devlin, M.-J., Oaknin, A., Kerger, J., López-Picazo, J.M., Machiels, J.-P., Delord, J.-P., Evans, T.R.J., Boni, V., Calvo, E., Topalian, S.L.,

Chen, T., Soumaoro, I., Li, B., Gu, J., Zwirtes, R., Moore, K.N., 2019. **Safety and Efficacy of Nivolumab Monotherapy in Recurrent or Metastatic Cervical, Vaginal, or Vulvar Carcinoma: Results From the Phase I/II CheckMate 358 Trial**. J. Clin. Oncol. JCO1900739. https://doi.org/10.1200/JCO.19.00739

68. Nicolle, R., Ayadi, M., Gomez-Brouchet, A., Armenoult, L., Banneau, G., Elarouci, N., Tallegas, M., Decouvelaere, A.-V., Aubert, S., Rédini, F., Marie, B., Labit-Bouvier, C., Reina, N., Karanian, M., le Nail, L.-R., Anract, P., Gouin, F., Larousserie, F., de Reyniès, A., de Pinieux, G., 2019. **Integrated molecular characterization of chondrosarcoma reveals critical determinants of disease progression**. Nat Commun 10, 4622. https://doi.org/10.1038/s41467-019-12525-7

69. Ordóñez, Y.F., Abad, J.L., Aseeri, M., Casas, J., Garcia, V., Casasampere, M., Schuchman, E.H., Levade, T., Delgado, A., Triola, G., Fabrias, G., 2019. **Activity-Based Imaging of Acid Ceramidase in Living Cells**. J. Am. Chem. Soc. https://doi.org/10.1021/jacs.8b11687

70. Oudard, S., Latorzeff, I., Caty, A., Miglianico, L., Sevin, E., Hardy-Bessard, A.C., Delva, R., Rolland, F., Mouret, L., Priou, F., Beuzeboc, P., Gravis, G., Linassier, C., Gomez, P., Voog, E., Muracciole, X., Abraham, C., Banu, E., Ferrero, J.-M., Ravaud, A., Krakowski, I., Lagrange, J.-L., Deplanque, G., Zylberait, D., Bozec, L., Houede, N., Culine, S., Elaidi, R., 2019. **Effect of Adding Docetaxel to Androgen-Deprivation Therapy in Patients With High-Risk Prostate Cancer With Rising Prostate-Specific Antigen Levels After Primary Local Therapy: A Randomized Clinical Trial.** JAMA Oncol. https://doi.org/10.1001/jamaoncol.2018.6607

71. Passet, M., Boissel, N., Sigaux, F., Saillard, C., Bargetzi, M., Ba, I., Thomas, X., Graux, C., Chalandon, Y., Leguay, T., Lengliné, E., Konopacki, J., Quentin, S., Delabesse, E., Lafage-Pochitaloff, M., Pastoret, C., Grardel, N., Asnafi, V., Lhéritier, V., Soulier, J., Dombret, H., Clappier, E., Group for Research on Adult ALL (GRAALL), 2019. **PAX5 P80R mutation identifies a novel subtype of B-cell precursor acute lymphoblastic leukemia with favorable outcome.** Blood 133, 280–284. https://doi.org/10.1182/blood-2018-10-882142

72. Perl, A.E., Martinelli, G., Cortes, J.E., Neubauer, A., Berman, E., Paolini, S., Montesinos, P., Baer, M.R., Larson, R.A., Ustun, C., Fabbiano, F., Erba, H.P., Di Stasi, A., Stuart, R., Olin, R., Kasner, M., Ciceri, F., Chou, W.-C., Podoltsev, N., Recher, C., Yokoyama, H., Hosono, N., Yoon, S.-S., Lee, J.-H., Pardee, T., Fathi, A.T., Liu, C., Hasabou, N., Liu, X., Bahceci, E., Levis, M.J., 2019**. Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML**. N. Engl. J. Med. 381, 1728–1740. https://doi.org/10.1056/NEJMoa1902688

73. Perrot, A., Lauwers-Cances, V., Tournay, E., Hulin, C., Chretien, M.-L., Royer, B., Dib, M., Decaux, O., Jaccard, A., Belhadj, K., Brechignac, S., Fontan, J., Voillat, L., Demarquette, H., Collet, P., Rodon, P., Sohn, C., Lifermann, F., Orsini-Piocelle, F., Richez, V., Mohty, M., Macro, M., Minvielle, S., Moreau, P., Leleu, X., Facon, T., Attal, M., Avet-Loiseau, H., Corre, J., 2019. **Development and Validation of a Cytogenetic Prognostic Index Predicting Survival in Multiple Myeloma**. J. Clin. Oncol. JCO1800776. https://doi.org/10.1200/JCO.18.00776

74. Pont, F., Tosolini, M., Fournié, J.J., 2019**. Single-Cell Signature Explorer for comprehensive visualization of single cell signatures across scRNA-seq datasets**. Nucleic Acids Res. https://doi.org/10.1093/nar/gkz601

75. Quinquenel, A., Fornecker, L.-M., Letestu, R., Ysebaert,L., Fleury, C., Lazarian, G., Dilhuydy, M.-S., Nollet, D., Guieze, R., Feugier, P., Roos-Weil, D., Willems, L., Michallet, A.-S., Delmer, A., Hormigos, K., Levy, V., Cymbalista, F., Baran-Marszak, F., 2019. **Prevalence of BTK and PLCG2 mutations in a real-life CLL cohort still on ibrutinib after three years: a FILO group study**. Blood. https://doi.org/10.1182/blood.2019000854

76. Ray-Coquard, I., Pautier, P., Pignata, S., Pérol, D., González-Martín, A., Berger, R., Fujiwara, K., Vergote, I., Colombo, N., Mäenpää, J., Selle, F., Sehouli, J., Lorusso, D., Guerra Alía, E.M., Reinthaller, A., Nagao, S., Lefeuvre-Plesse, C., Canzler, U., Scambia, G., Lortholary, A., Marmé, F., Combe, P., de Gregorio, N., Rodrigues, M., Buderath, P., Dubot, C., Burges, A., You, B., Pujade-Lauraine, E., Harter, P., PAOLA-1 Investigators, 2019. **Olaparib plus Bevacizumab as First-Line Maintenance in Ovarian Cancer**. N. Engl. J. Med. 381, 2416–2428. https://doi.org/10.1056/NEJMoa1911361

77. Rieu, J.-B., Vergez, F., 2019a. **Marked lymphocytosis and atypical cells with a cleft nucleus in a 1-month-old child.** Blood 134, 216. https://doi.org/10.1182/blood.2019001433

78. Rieu, J.-B., Vergez, F., 2019b. **Never judge a book by itscover: these neutrophils are not reactive!** Blood 134, 656. https://doi.org/10.1182/blood.2019001640

79. Rini, B.I., Plimack, E.R., Stus, V., Gafanov, R., Hawkins, R., Nosov, D., Pouliot, F., Alekseev, B., Soulières, D., Melichar, B., Vynnychenko, I., Kryzhanivska, A., Bondarenko, I., Azevedo, S.J., Borchiellini, D., Szczylik, C., Markus, M., McDermott, R.S., Bedke, J., Tartas, S., Chang, Y.-H., Tamada, S., Shou, Q., Perini, R.F., Chen, M., Atkins, M.B., Powles, T., KEYNOTE-426 Investigators, 2019. **Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma.** N. Engl. J. Med. 380, 1116–1127. https://doi.org/10.1056/NEJMoa1816714

80. Ruhstaller, T., Giobbie-Hurder, A., Colleoni, M., Jensen, M.-B., Ejlertsen, B., de Azambuja, E., Neven, P., Láng, I., Jakobsen, E.H., Gladieff, L., Bonnefoi, H., Harvey, V.J., Spazzapan, S., Tondini, C., Del Mastro, L., Veyret, C., Simoncini, E., Gianni, L., Rochlitz, C., Kralidis, E., Zaman, K., Jassem, J., Piccart-Gebhart, M., Di Leo, A., Gelber, R.D., Coates, A.S.,

Goldhirsch, A., Thürlimann, B., Regan, M.M., members of the BIG 1-98 Collaborative Group and the International Breast Cancer Study Group, 2019. **Adjuvant Letrozole and Tamoxifen Alone or Sequentially for Postmenopausal Women with Hormone Receptor-Positive Breast Cancer: Long-Term Follow-Up of the BIG 1-98 Trial**. J. Clin. Oncol. 37, 105–114. https://doi.org/10.1200/JCO.18.00440

81. G., Slack, G.W., Telenius, A., Miyata-Takata, T., Viganò,E., Molina, T.J., Damotte, D., Ben-Neriah, S., Copie-Bergman, C., Laurent, C., Mottok, A., Salles, G., Savage, K.J., Scott, D.W., Traverse-Glehen, A., Steidl, C., 2019. **Mutational Landscape of Grey Zone Lymphoma.** Blood 134, 21. https://doi.org/10.1182/blood-2019-127375

82. Scherpereel, A., Mazieres, J., Greillier, L., Lantuejoul, S., Dô, P., Bylicki, O., Monnet, I., Corre, R., Audigier-Valette, C., Locatelli-Sanchez, M., Molinier, O., Guisier, F., Urban, T., Ligeza-Poisson, C., Planchard, D., Amour, E., Morin, F., Moro-Sibilot, D., Zalcman, G., French Cooperative Thoracic Intergroup, 2019. **Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial**. Lancet Oncol. 20, 239–253. https://doi.org/10.1016/S1470-2045(18)30765-4

83. Siu, L.L., Even, C., Mesía, R., Remenar, E., Daste, A., Delord, J.-P., Krauss, J., Saba, N.F., Nabell, L., Ready, N.E., Braña, I., Kotecki, N., Zandberg, D.P., Gilbert, J., Mehanna, H., Bonomi, M., Jarkowski, A., Melillo, G., Armstrong, J.M., Wildsmith, S., Fayette, J., 2019. **Safety and Efficacy of Durvalumab With or Without Tremelimumab in Patients With PD-L1-Low/Negative Recurrent or Metastatic HNSCC: The Phase 2 CONDOR Randomized Clinical Trial.** JAMA Oncol 5, 195–203. https://doi.org/10.1001/jamaoncol.2018.4628

84. Smith, C.C., Levis, M.J., Perl, A.E., Martinelli, G., Neubauer, A., Berman, E., Montesinos, P., Baer, M.R., Larson, R.A., Chou, W.-C., Yokoyama, H., Recher, C., Yoon, S.-S., Hill, J.E., Rosales, M., Bahceci, E., 2019. **Emerging Mutations at Relapse in Patients with FLT3-Mutated Relapsed/Refractory Acute Myeloid Leukemia Who Received Gilteritinib Therapy in the Phase 3 Admiral Trial.** Blood 134, 14. https://doi.org/10.1182/blood-2019-122620

85. Stuani, L., Sarry, J.-E., 2019. **Help from outside: cystine to survive in AML.** Blood 134, 336–338. https://doi.org/10.1182/blood.2019001580

86. Surun, A., Varlet, P., Brugières, L., Lacour, B., Faure-Conter, C., Leblond, P., Bertozzi-Salomon, A.-I., Berger, C., André, N., Sariban, E., Raimbault, S., Prieur, F., Desseigne, F., Zattara, H., Guimbaud, R., Polivka, M., Delisle, M.-B., Vasiljevic, A., Maurage, C.-A., Figarella-Branger, D., Coulet, F., Guerrini-Rousseau, L., Alapetite, C., Dufour, C., Colas, C., Doz, F., Bourdeaut, F., 2019. **Medulloblastomas associated with APC germline pathogenic variant share the good prognosis of CTNNB1 mutated medulloblastomas**. Neuro-oncology. https://doi.org/10.1093/neuonc/noz154 **IF 10.091**

87. Thakurta, A., Ortiz, M., Blecua, P., Towfic, F., Corre, J., Serbina, N.V., Flynt, E., Yu, Z., Yang, Z., Palumbo, A., Dimopoulos, M.A., Guttierez, N., Goldschmidt, H., Sonneveld, P., Avet-Loiseau, H., 2019. **High sub-clonal fraction of 17p deletion is associated with poor prognosis in Multiple Myeloma**. Blood. https://doi.org/10.1182/blood-2018-10-880831

88. Toulmonde, M., Pulido, M., Ray-Coquard, I., Andre, T., Isambert, N., Chevreau, C., Penel, N., Bompas, E., Saada, E., Bertucci, F., Lebbe, C., Le Cesne, A., Soulie, P., Piperno-Neumann, S., Sweet, S., Cecchi, F., Hembrough, T., Bellera, C., Kind, M., Crombe, A., Lucchesi, C., Le Loarer, F., Blay, J.-Y., Italiano, A., 2019. **Pazopanib or methotrexate-vinblastine combination chemotherapy in adult patients with progressive desmoid tumours (DESMOPAZ): a non-comparative, randomised, open-label, multicentre, phase 2 study**. Lancet Oncol. https://doi.org/10.1016/S1470-2045(19)30276-1

89. Uro-Coste, E., Masliah-Planchon, J., Siegfried, A., Blanluet, M., Lambo, S., Kool, M., Roujeau, T., Boetto, S., Palenzuela, G., Bertozzi, A.-I., Gambart, M., Coupier, I., Oliver-Petit, I., Golmard, L., Julia, S., Savagner, F., Mohand-Oumoussa, B., Tauziede-Espariat, A., Delisle, M.-B., Figarella-Branger, D., Bourdeaut, F., Rigau, V., 2019. **ETMR-like infantile cerebellar embryonal tumors in the extended morphologic spectrum of DICER1-related tumors**. Acta Neuropathol. 137, 175–177. https://doi.org/10.1007/s00401-018-1935-7

90. Valentin, T., Lesluyes, T., Le Guellec, S., Chibon, F., 2019. **Chemotherapy in localized soft tissue sarcoma: will we soon have to treat grade 1 tumors? Update on CINSARC performances.** Ann. Oncol. 30, 153–155. https://doi.org/10.1093/annonc/mdy465

91. Vitiello, G.A., Bowler, T.G., Liu, M., Medina, B.D., Zhang, J.Q., Param, N.J., Loo, J.K., Goldfeder, R.L., Chibon, F., Rossi, F., Zeng, S., DeMatteo, R.P., 2019. **Differential immune profiles distinguish the mutational subtypes of gastrointestinal stromal tumor.** J. Clin. Invest. https://doi.org/10.1172/JCI124108

92. Walter, O., Treiner, E., Bonneville, F., Mengelle, C., Vergez, F., Lerebours, F., Delobel, P., Liblau, R., Martin-Blondel, G., Immune Checkpoint Inhibitors in PML Study Group, 2019. **Treatment of Progressive Multifocal Leukoencephalopathy with Nivolumab.** N. Engl. J. Med. https://doi.org/10.1056/NEJMc1816198

93. Ysebaert, L., 2019. **On the BALL to spot the best score able to predict overall survival in relapsed or refractory CLL**. Lancet Haematol. https://doi.org/10.1016/S2352-3026(19)30091-2


Inserm
cnrs
FHF
CRCT
unicancer
UNIVERSITÉ TOULOUSE III PAUL SABATIER
ars
UNICANCER
CLAUDIUS REGAUD
Hôpitaux de Toulouse

IUCT-Oncopole
1 avenue Irène Joliot-Curie
31059 Toulouse cedex 9
+ 33 (0) 5 31 15 50 50
www.iuct-oncopole.fr

Follow us on: