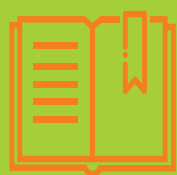


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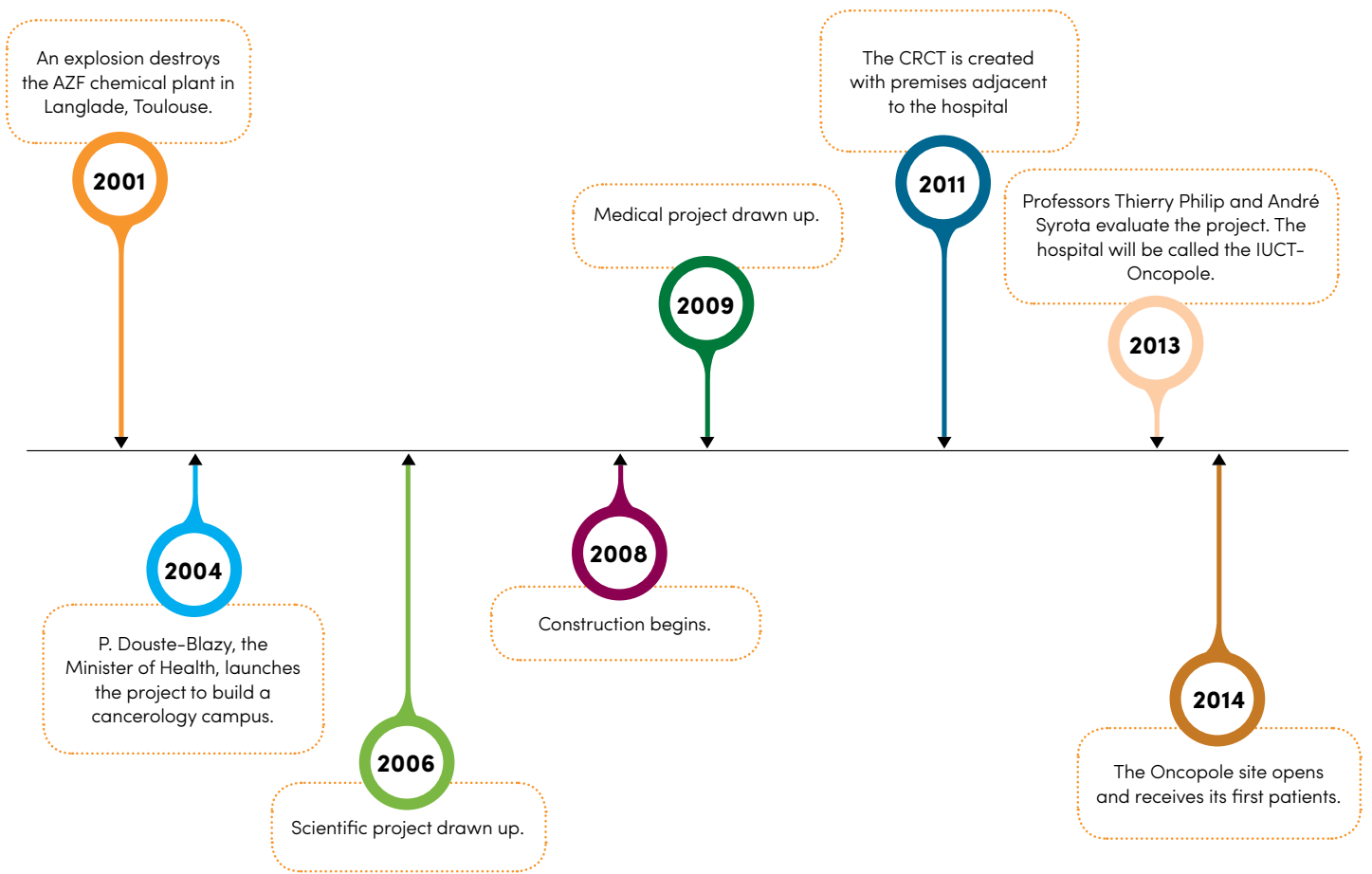
TOULOUSE UNIVERSITY
CANCER INSTITUTE—ONCOPOLE

—
2018



INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
Oncopole

Project timeline



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 department, the Institut Claudius Regaud (French comprehensive care 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 1,800 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 1,500 people to benefit from innovative therapies in 2018. In addition, combining both medical and scientific expertise within most of the site's basic research teams has proved to be a powerful driver of innovation all along the treatment-research continuum.

This reports presents the results achieved by the IUCT-Oncopole in 2018.

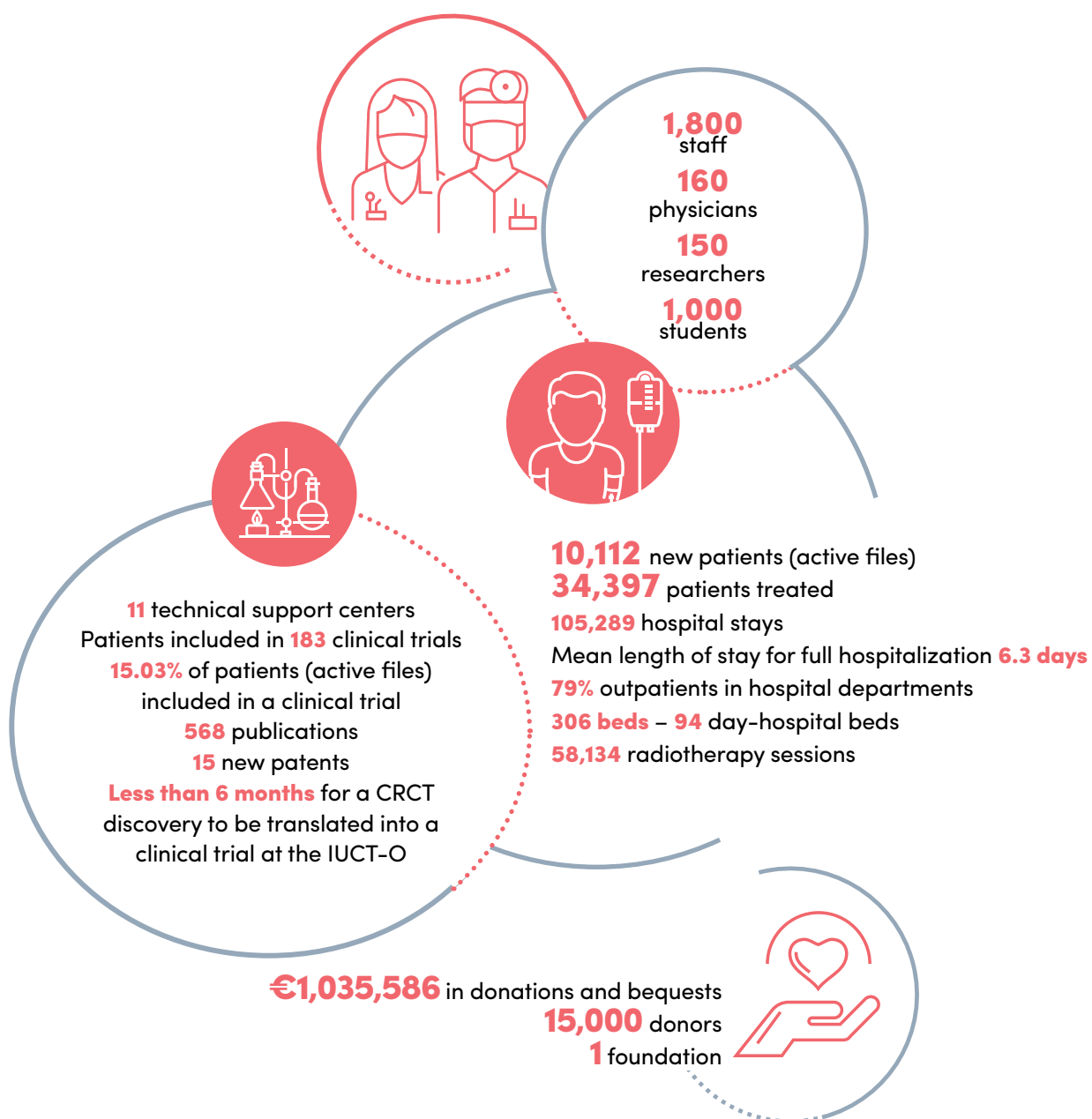
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KEY FIGURES

2018





Prof. Michel Attal,
General Manager of the IUCT-Oncopole

“A diversity of expertise drives innovation”

The IUCT-Oncopole is 5 years old. We have successfully brought together the expertise of the site's three establishments – the Institut Claudius Regaud, Toulouse University Hospital's oncology teams and the CRCT's research teams – within a model that promotes the cross-fertilization of ideas from a wide variety of fields. Combining such a diversity of expertise drives innovation.

Our publication rate – more than 550 papers per year – and the ever-growing number of innovative treatments developed at the IUCT-Oncopole show that integrating research into treatment has been a great success.

A new phase is about to begin. As we come to the end of the launch phase, with its high growth rates in every field, we are looking towards a new set of medical-scientific objectives, which we will define in the summer of 2019, taking into account both our achievements and advances in science. This will lead to a new roadmap for

the IUCT-Oncopole centered round restructuring three areas that have grown substantially – consultations, the hospitalization department and the clinical research department. The advent of personalized medicine has raised a need for new patient pathways. In fact, treating cancer is a complex process that calls upon ever-more specialized skills. What is more, the expansion of outpatient therapies is forcing us to rethink the way we coordinate treatment between the hospital and the patient's home.

If we are to meet these challenges, we will have to extend our premises and expand our capabilities by welcoming new research teams.

In 2018, we applied for OEI accreditation. Our scientific output is remarkable, in terms of both quality and quantity (568 publications in 2018). Our goal is to strengthen and valorize this output still further through national and international partnerships.



Marc Penaud, General Manager of Toulouse University Hospital

Working together to meet several major challenges

Five years have gone by since the Toulouse University Cancer Institute-Oncopole, the only institution of its kind in France, opened at Langlade. And since 2014, we have all been working towards a single objective – to drive back cancer and perhaps, in the future, overcome it. Learning more about cancer is the only way to improve our ability to combat it and give people hope.

Over the last five years, our staff have worked together to overcome several major challenges:

- Combine the strengths of a cancer care and research center, the Institut Claude Regaud, and Toulouse University Hospital;
- Reorganize public-sector cancer treatment and research in the Toulouse area;
- Create direct links between researchers and clinicians, and ensure patients benefit from the lat-

est advances in cancer treatment by integrating a cancer research center, the CRCT, into the hospital;

- Set up a regional cancer treatment network with our partners so every patient receives the highest quality treatment as close as possible to his or her home;
- Advise and assist patients through every aspect of cancer treatment.

Uniting the strengths of Toulouse University Hospital and the Institut Claude Regaud at the Oncopole, Purpan and Rangueil-Larrey sites has been a great success in terms of combating cancer, as can be seen from the facts and figures contained in our 2018 Activity Report.

I would like to take this opportunity to thank everyone involved for their work helping patients and their commitment to fighting cancer.

“The IUCT-Oncopole is consolidating its position”

New research teams, a significant increase in publications in high-impact journals, perspectives and challenges: a conversation with Jean-Pierre Delord, the IUCT-Oncopole’s Director of Medical Affairs, and Gilles Favre, Director of the CRCT.

How would you sum up the past year?

Jean-Pierre Delord: 2018 was a period of consolidation for the IUCT-Oncopole. In the case of patients and our colleagues in the Midi-Pyrenees area, this involved strengthening our role as a regional hospital. For example, we saw a truly spectacular increase in the number of patients we included in clinical research programs. On a national level, we continued moving forward by renewing existing accreditations, obtaining new certifications and increasing the number of collaborations between researchers and physicians. We also made progress towards our aim of establishing Toulouse as an internationally renowned cancer center. There is fierce competition, but I believe we are well on the way to achieving this goal.

Gilles Favre: One sign of this recognition is our extremely high publication rate, which, for the first time, exceeded one-and-a-half publications per day in 2018. This achievement justifies the resources allocated and shows our ability to attract top quality research teams.

What were the year’s key events?

Jean-Pierre Delord: On the one hand, we have our brilliant and internationally respected research teams, which continued demonstrating their extraordinary abilities. On the other hand, we have taken steps to expand other areas of research by recruiting new teams, such as Frédéric Chibon’s sarcoma team, which joined the CRCT less than two years ago. Successful applications for PHRC, PRT-K and PHRI grants in 2018 will enable his team to continue improving our understanding of this complex disease.

Gilles Favre: I am also thinking of Salvatore Valitutti, whose team joined the CRCT in 2018, and Vera Pancaldi, an expert in the biology of systems, who was appointed to head the first Chair of Bio-Informatics in Oncology, created with funding from the Fondation Toulouse Cancer Santé, Inserm and the Pierre Fabre Research Institute. This brought the total number of CRCT research teams to 21. 2018 also saw the inclusion of the first patients in a clinical trial to test a combined anti-inflammatory-immunotherapy treatment



Professors Gilles Favre and Jean-Pierre Delord

PHRC:

Hospital Clinical Research Program

PRT-K:

Translational Cancer Research Program

PHRI:

Hospital Nursing Research Program



for melanomas. This trial, based on the results of research carried out at the CRCT by Bruno Ségui and Nicolas Meyer, provides yet another example of how the IUCT-Oncopole facilitates the transfer of basic research to clinical trials.

What is in store for 2019?

Jean-Pierre Delord: We already need to expand both our facilities and our healthcare offer, so our teams can continue to work effectively and so we can maintain our all-important ability to pass on the benefits of our research to patients. With this in mind, we are drawing up plans to extend our premises. In addition, given the impact of new technologies on both

patient care and research, we need to improve our ability to connect with the “hard” sciences, especially by increasing our computing power and the power of our mathematical models. Deciphering the complexity of living organisms obviously requires cutting-edge basic research, but progress in this area cannot be made without powerful tools, such as artificial intelligence.

Gilles Favre: 2019 will see the concretization of our alliance with Laboratoires Pierre Fabre, when France’s High Council for the Evaluation of Research and Higher Education assesses the partnership. Our aim is to join Europe’s main consortiums and form partnerships with international research centers.

HIGHLIGHTS OF 2018

JANUARY

A new dental-hygiene consultation service

Dental hygiene consultations are now provided to all radiotherapy patients and to other inpatients on request from healthcare teams. Consultations take place immediately prior to treatment and during the post-treatment monitoring phase.

1st Issue of our Research newsletter

This IUCT-Oncopole's new monthly newsletter will keep staff up to date with the site's research activities (publications, funding, etc.).

MARCH

Supportive Care Tour de France

The "Grand Départ" of the Supportive Care Tour de France (AFSOS), hosted by the IUCT-Oncopole, enabled more than 100 patients to take part in 14 workshops run by supportive care professionals.

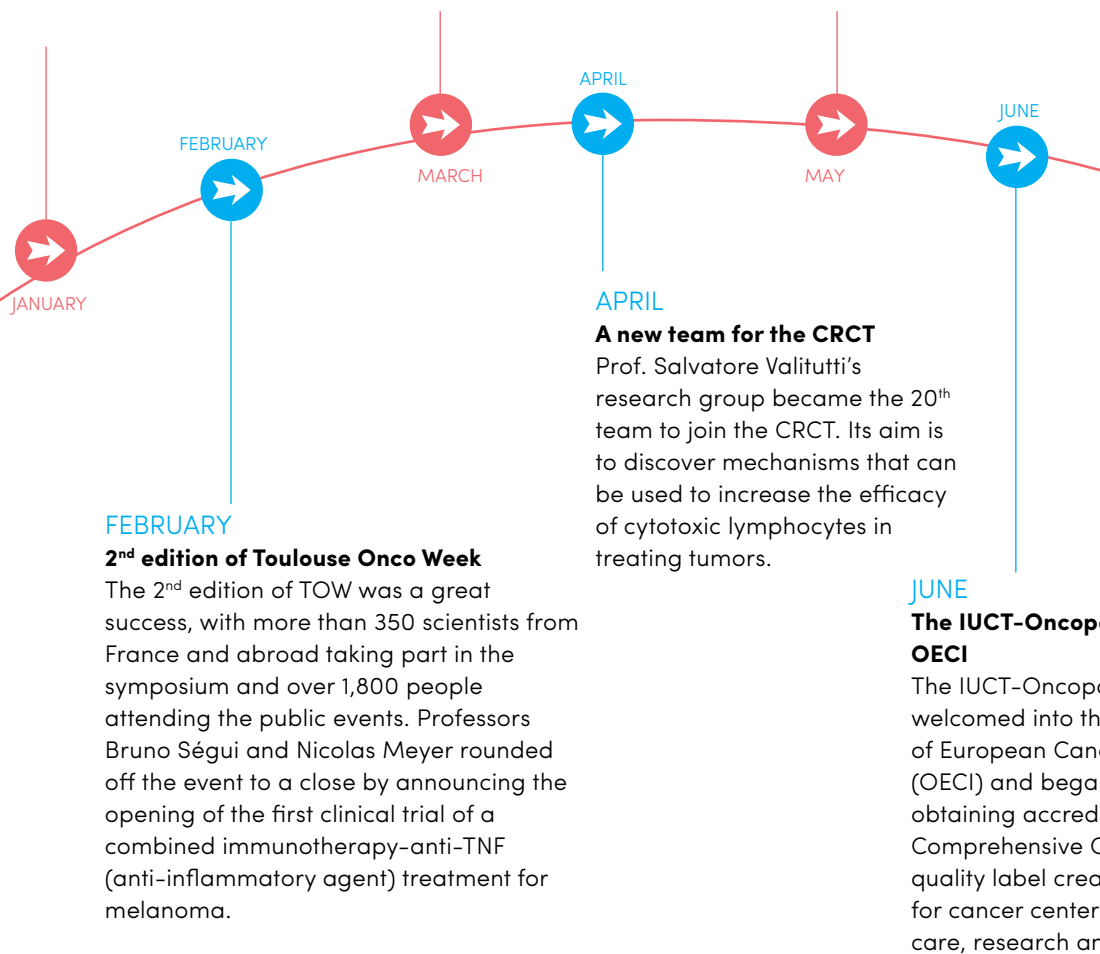
CRCT Team 12 on the front cover of Le Point

Le Point magazine put Dr. Marc Poirot and Dr. Sandrine Silvente-Poirot on the front cover of its March 29, 2018 issue in recognition of their work on breast cancer.

MAY

Dual certification for the CRCT's technology cluster

The CRCT's technology cluster received dual ISO9001:2015/NFX 50-900 certification for "its expertise and technological R&D in genomics and transcriptomics, proteomics, vectorology, cellular, cytometric and tri-cellular imaging, bioinformatics, antibody production and as a biological resource center".





JULY

Toulouse hosts the ESOF

Hosting the 8th EuroScience Open Forum (ESOF) made Toulouse the “European City of Science”. Fifteen science journalists from around the world visited the IUCT-Oncopole and CRCT during the event.



JULY

AUGUST

AUGUST

Creation of the Cancerology UTEP

The Regional Health Agency chose the IUCT-Oncopole to be the “sponsor and guarantor of the Transversal Unit for Therapeutic Education (UTEP) specializing in cancerology for the Occitanie Region”. The UTEP was created as part of the Occitanie 2022 Regional Health Project.

SEPTEMBER

A new breast reconstruction technique

Dr. Gabrielle Selmes performed the first breast reconstruction with latissimus dorsi flap to be carried out in the region.

Launch of the 1st Chair of Bio-Informatics in Oncology

Dr. Vera Pancaldi was chosen to head the first chair of Bio-Informatics in Oncology, set up with funding from the Fondation Toulouse Cancer Santé, the Pierre Fabre Research Institute, and Inserm. Dr. Pancaldi’s new team became the CRCT’s 21st research team.

SEPTEMBER

OCTOBER

OCTOBER

The IUCT-Oncopole joins forces with Stade Toulousain Rugby Club

The IUCT-Oncopole and Stade Toulousain Rugby Club have joined forces to encourage patients to stay active. With expertise provided by the Sport and Health CAMI and support from Malakoff-Médéric, the two organizations launched a sports therapy program at Ernest Wallon Stadium.

350 patients attend the 3rd ‘Life After Cancer’ Day

The 3rd Life After Cancer Day gave patients an opportunity to sample 14 different well-being workshops (Sophrology, Qi gong, Pink Pilates, Afropop dance, etc.).

NOVEMBER

Innovative plastic surgery procedure

Dr. Karim Kolsi carried out the first ganglion transplant operation to treat a refractory lymphoedema. The IUCT-Oncopole is one of only three centers in France to offer this technique.

NOVEMBER

DÉCEMBER

DECEMBER

National calls for projects: 5 projects selected

The General Directorate for Healthcare services (DGOS) awarded 4 grants to IUCT-Oncopole research projects, including 2 PHRC-K grants (BLAD-RAD001 and CHIC-ST5 01 projects) and 2 PRTK grants (MIRAS-SARRA and LUNG RESIST projects).

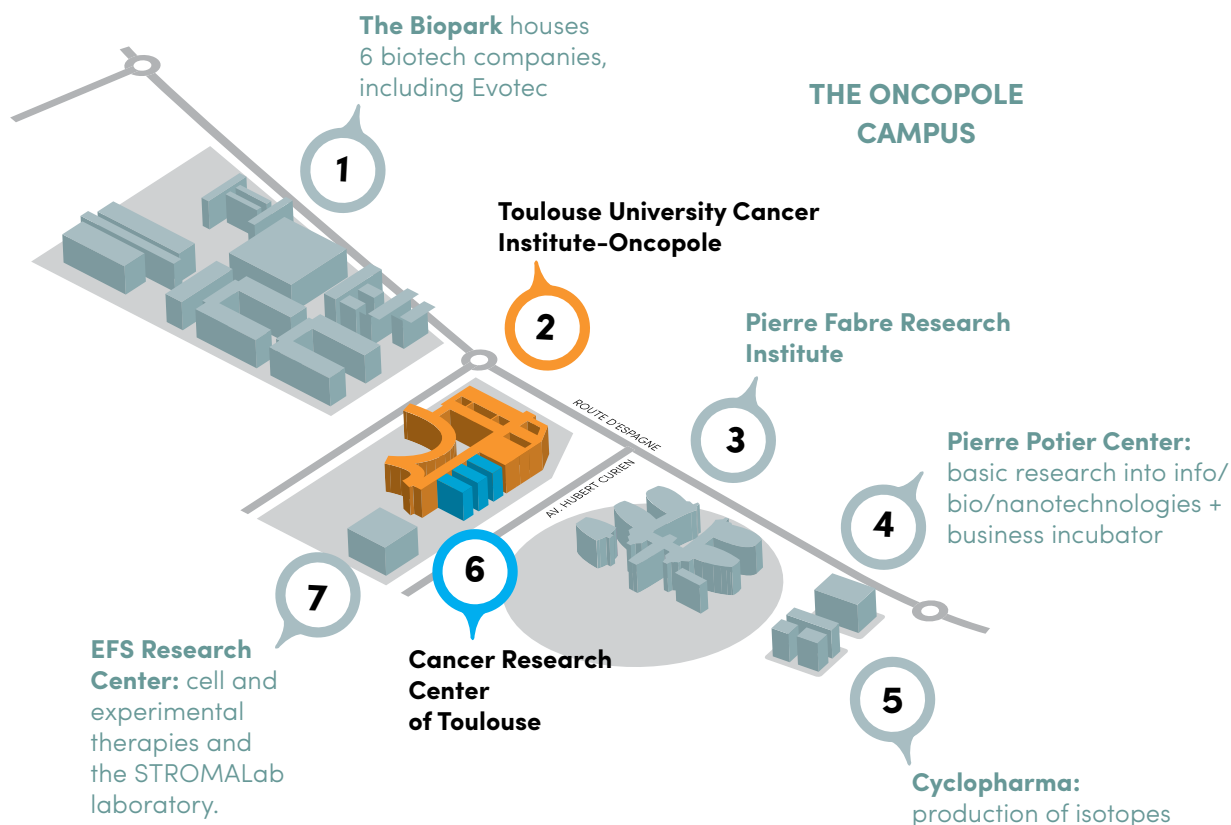
Signature of an agreement with the Fondation Toulouse Cancer Santé

The IUCT-Oncopole, via the ICR, is now a founder member of the Fondation Toulouse Cancer Santé.



A REFERENCE CENTER
AT THE HEART OF NETWORKS

A single site



The Oncopole Campus

Toulouse Oncopole 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.

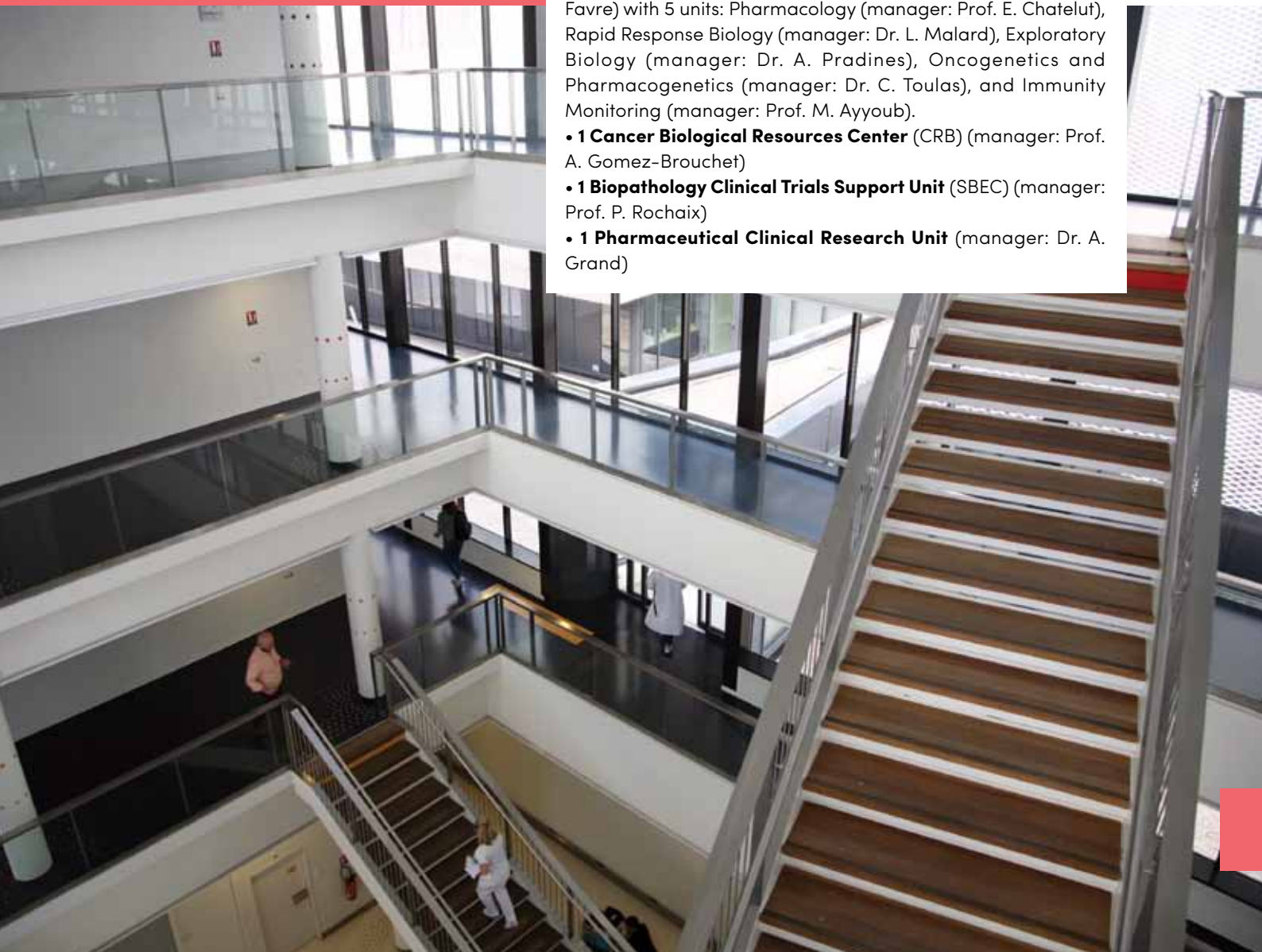
A Community Center close to the IUCT-Oncopole provides a variety of services to patients (*départementale* branch of the Ligue Contre le Cancer, specialist hair-dressing salon, adapted physical activities, etc.). An aftercare and rehabilitation clinic is currently being built on the site and should welcome its first patients by 2020.

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. It also allows many services, laboratories and units in the "care-research continuum" to be shared:

- **1 Technology Cluster** with 8 technical services units (manager: F. Lopez)
- **1 Preclinical Trials Center** – CREFRE-US006 (director: Dr. Y. Barreira)
- **1 Pathology Laboratory** with 30 practitioners (manager: Prof. P. Brousset)
- **1 Onco-Hematology Transfer Platform** with 2 research units: myeloma genomics (manager: Prof. H. Avet-Loiseau) and acute leukemia (manager: Prof. E. Delabesse)
- **1 Oncology Medical Biology Laboratory** (manager: Prof. Gilles 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).
- **1 Cancer Biological Resources Center** (CRB) (manager: Prof. A. Gomez-Brouchet)
- **1 Biopathology Clinical Trials Support Unit** (SBEC) (manager: Prof. P. Rochaix)
- **1 Pharmaceutical Clinical Research Unit** (manager: Dr. A. Grand)

The "Exchanges Walkway" links the CRCT to the IUCT-Oncopole.



Sustainable development at the IUCT-Oncopole

The Oncopole campus was built on brownfield land and is gradually being incorporated into Toulouse Metropolitan Council's sustainable development dynamic. A 2.5-km greenway runs beside the Garonne River from the Oncopole to the Prairie des Filtres, providing a traffic-free route to the city center for pedestrians and cyclists, while the new Urbain Sud cable car, due to open at the end of 2020, 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. The campus will also have its own solar power plant by 2020, built with support from the Ministry for Environmental Transition and Solidarity's Energy Regulation Commission. The plant's 35,000 solar panels 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 Castillonaise sheep have grazed 3,000 m² of grass since 2017) and installing beehives on the building's roofs (they produce between 30 and 50 kg of honey per year).



The IUCT-Oncopole's grounds



Structure

Governance of the site has been strengthened by setting up a Strategy Council, a joint Scientific Directorate for the hospital and research center, and a Scientific Advisory Board.

All translational research programs are steered jointly by a physician and a researcher.

The three IUCTs: Oncopole, Purpan, Rangueil/Larrey

Combining their strengths enables the Institut Claudius Regaud (ICR) and CHU-Toulouse University Hospital's oncology departments 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
- Urology (medical and innovative surgery)
- Head and neck cancers
- Skin cancers: melanomas
- Sarcomas
- Neuro-oncology
- Thyroid cancers and neuroendocrine tumors
- Oncogenetics
- Geriatric oncology (shared service)
- Radiotherapy
- Nuclear medicine and brachytherapy



INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
Purpan

- Bone cancers
- Cancers of the nervous system
- Geriatric oncology (shared service)
- 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

Oncopole: a trademark registered by Toulouse Metropolitan Council to designate the campus built on the site destroyed by the AZF chemical plant explosion in 2001.

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-Ranguueil/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 regional cancerology network (now Onco-Occitanie), the Ligue Contre le Cancer and the Fondation Toulouse Cancer Santé.

CUC: the GCS set up to build the hospital. It comprises the Institut Claudius Regaud, Toulouse University Hospital, the Midi-Pyrénées private-sector cancerology GCS, the French Blood Service, the Oncomip regional cancerology network and the GCS covering the area's general hospitals.

Care organized 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 12 OCCs:

- Breast Cancer OCC
Coordinators: Prof. Florence Dalenc
– Dr. Eva Jouve – Dr. Charlotte Vaysse
- Gynecology OCC
Coordinator: 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
Coordinators: Prof. Rosine Guimbaud
– Dr. Vivianne Feillel
- Oncogeriatrics OCC
Coordinators: Dr. Loïc Mourey – Dr. Laurent Balardy
- Supportive Care OCC
Coordinators: Dr. Nathalie Caunes-Hilary
– Dr. Virginie Woisard
- Hematology OCC
Coordinator: Prof. Christian Récher
- Thyroid and Neuroendocrine Cancers OCC
Coordinators: Prof. Frédéric Courbon – Prof. Rosine Guimbaud – Prof. Delphine Vezzosi.

List of the 3 associate OCCs:

- 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



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, Sébastien MASSIP*

Executive Council

Prof. Michel Attal
Prof. Odile Beyne-Rauzy
Prof. Pierre Brousset
Prof. Jean-Pierre Delord
Prof. Gilles Favre
Dr. Sébastien Pierre**
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

Consultations

Hematology

Prof. Christian RECHER

Internal Medicine

Prof. Odile BEYNE-RAUZY

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

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

Prof. Rosine GUIMBAUD


Oncogenetics

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

* replaced by Elvis CORDIER in 2019

** replaced by Dr. Nathalie CAUNES-HILARY in 2019

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.

Onco-Occitanie

Onco-Occitanie is the name of the new regional cancer network that came into being when the OncoLR and Oncomip networks merged following the creation of the Occitanie Region in 2015. As well as coordinating cancer treatment across the region, Onco-Occitanie distributes reference documents and follow-up protocols, and supports the actions of the region's healthcare professionals. In addition, it manages and updates a medical record sharing mechanism (*Dossier Communicant de Cancérologie*), coordinates the work of cancer care coordination centers, and helps evaluate the quality of cancer care. It also organizes annual briefings, held at the IUCT-Oncopole, for professionals involved in the fight against cancer.

www.onco-occitanie.fr/

Cancéropôle Grand Sud-Ouest (GSO)

Cancéropôle GSO is a group 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. Cancéropôle is a dynamic cancer research network that provides funding for promising projects in the fight against cancer and organizes numerous scientific events.

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 order (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 is composed of 13 internationally respected researchers and physicians:

- Maria Blasco, Centro Nacional de Investigaciones Oncológicas – Madrid, Spain
- Patrick Couvreur, Paris-Sud University – Paris, France
- Anne Dejean, Institut Pasteur – Paris, France
- Jean-Marc Egly, Institute of Genetics and Molecular



and Cellular Biology – Strasbourg, France

- Benoit Van den Eynde, Ludwig Institute – Brussels, Belgium
- Bruno Goud, Institut Curie – Paris, France
- John A. Hickma, IMI Coordinator – Paris, France
- Liselotte Højgaard, Rigshospitalet, University of Copenhagen – Copenhagen, Denmark
- Cyril M. Kay, University of Alberta – Edmonton, Canada
- Gillies McKenna, Oxford Institute for Radiation Oncology – Oxford, United Kingdom
- Jacques Pouysségur, Institute for Research on Cancer and Aging – Nice, France
- Josep Tabernero, Vall d'Hebron Institute of Oncology – Barcelona, Spain
- William Vainchenker, Gustave Roussy – Villejuif, France

One of the Scientific Advisory Board's most important tasks is to evaluate projects applying for @IUCT funding and to select those that will be carried out at the IUCT-Oncopole and the CRCT.

www.iuct.fr

Fondation Toulouse Cancer Santé

Amgen, GSK GlaxoSmithKline, Pierre Fabre, Siemens, Total and the Institut Claude Regaud set up the Fondation Toulouse Cancer Santé-Innabiosanté in order to promote research and improve knowledge in the field of healthcare technology, especially in relation to cancer. Awarded "public utility" status by ministerial decree on May 5, 2006, its initiatives include providing funding for innovative, interdisciplinary and collaborative projects submitted by members of the Toulouse area's medical-scientific community. This funding is designed to encourage research teams to present the sort of high-risk projects that may lead to tomorrow's scientific, technological and economic breakthroughs. The Fondation Toulouse Cancer Santé and the IUCT GIP have the same Scientific Council.

www.toulousecancer.fr

The Fondation Toulouse Cancer Santé is a founding partner of the Summer School on Medicines (SSM). This annual event, created in conjunction with Barcelona Science Park (PCB) and the University of Montreal, provides master's, doctoral and post-doctoral level science students, including medical and pharmacy students, with a detailed introduction to the complex process of drug R&D, from original discovery to preclinical and clinical trials to market launch. The 10th SSM took place in Ribeiro Preto (state of Sao Paulo) in Brazil, from March 16 to 23, 2018. For its most recent initiative, the Fondation Toulouse Cancer Santé has chosen the field of bioinformatics, with the aim of harnessing the latest technological advances in order to process the "big data" produced by clinical trials and research projects. Efficient data processing is essential if patients are to benefit from the results of studies as quickly as possible. To this end, the FTCS, in conjunction with the Pierre Fabre Research Institute, has created the first Chair of Bio-Informatics in Oncology, which is led by Dr. Vera Pancaldi, the head of CRCT team 21.

Etablissement Français du Sang (EFS - French Blood Service)

EFS facilities on the Oncopole site include:

- 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 (samples taken in 2018: 176 autologous HSC, 42 allogenic HSC and 9 lymphocyte/cell).
- 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' requirements, the unit also responds to requests from other centers in the region, France and abroad (transfers in 2018: 144 autologous HSC, 70 allogenic HSC, 13 bone marrow and 28 mononucleated cells/3,109 grafts stored in liquid nitrogen).
- Institute of Regenerative Medicine, which also houses Stromalab, a mixed research unit that focuses on the role and functions of stem cells, including mesenchymal bone marrow cells and adipose tissues, and their use in regenerative medicine.

www.efs.sante.fr

www.stromalab.fr/en

National and international networks

The IUCT-Oncopole is a national center of expertise for more than 15 INCa networks and a member of two international networks of excellence – proof of the quality of its healthcare and research activities.

UNICANCER

The IUCT-Oncopole, through the Institut Claudius Regaud, is a member of the UNICANCER group of 18 French Comprehensive Cancer Centers (FCCC). FCCCs are private, nonprofit healthcare providers that contribute to France's public hospital service with the aim of improving the quality and accessibility of cancer care. The IUCT-Oncopole is highly involved in several specialist groups, most notably the Oncoimmunology Group (GIO), which was set up in December 2016 with Prof. J-P. Delord as vice-president. Prof. Delord is also a member of UNICANCER's Scientific and Strategic Council.

www.unicancer.fr

Fédération Hospitalière de France (FHF)

The IUCT-Oncopole, through Toulouse University Hospital, is a member of the Fédération Hospitalière de France (FHF). Created in 1924, the FHF represents almost all of France's public-sector healthcare establishments, including more than 1,000 public hospitals and a similar number of medico-social establishments (retirement homes and specialist care homes). The FHF has three main roles: promotion, information and representation.

www.fhf.fr



INCa-accredited national referral networks

The IUCT-Oncopole is a regional referral center for nine rare cancers:

- **CARADERM**: rare skin cancers (contact: Prof. N. Meyer)
- **CARARE**: rare kidney cancers (contact: Dr. C. Chevreau)
- **NETSARC**: soft tissue and visceral sarcomas (contact: Dr. C. Chevreau)
- **POLA**: high-grade oligodendrogliomas (contact: Prof. E. Moyal)
- **REF-COR**: rare head and neck cancers (contact: Prof. S. Vergez)
- **RENAPE**: rare peritoneal cancers (contact: Dr. G. Ferron)
- **RESOS**: bone sarcomas (contact: Dr. C. Chevreau)
- **TMRO**: rare ovarian cancers (contact: Dr. G. Ferron)
- **TUTHYREF**: refractory thyroid cancers (contact: Dr. S Zerdoud)

It is also a regional pathology referral 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. P. Rochaix)
- **TENpath**: rare neuroendocrine tumors (contact: Dr. M. Danjoux)

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

- **CLIP²**: early phase clinical trials centers (contact: Prof. J-P. Delord)
- **GINECO**: national investigation groups for the study of ovarian and breast cancers (contact: Dr. L. Gladiéff)
- **LYSA**: collaborative clinical and translational research group on lymphoma (contact: Prof. C. Laurent)
- **RADIOTRANSNET**: preclinical radiotherapy research in France (contact: Prof. E. Moyal)

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 purpose 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.

Organisation of European Cancer Institutes (OEI)

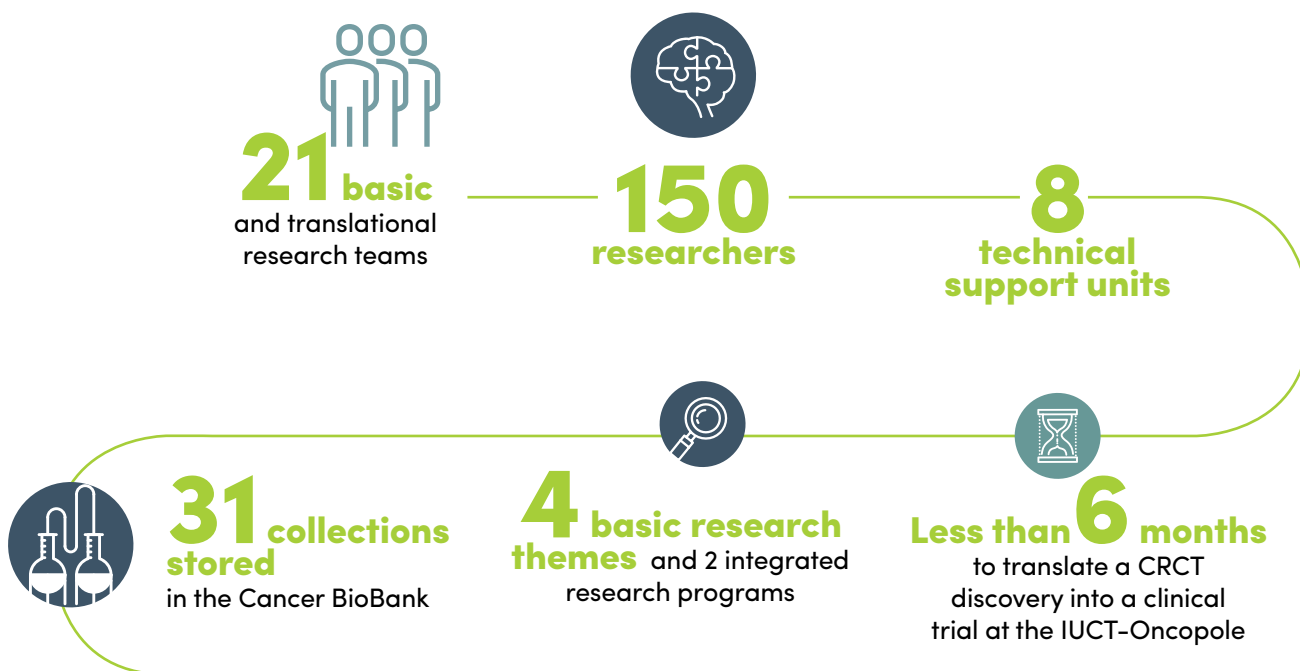
Since 2018, the IUCT-Oncopole has been a member of the OEI network of cancer centers, which was set up in order to create a critical mass of expertise and skills that would further the development of personalized treatment. Its 82 members, 11 of which are in France, work together to ensure patients throughout Europe have access to the best possible treatment. The IUCT-Oncopole is currently going through the Comprehensive Cancer Center accreditation process



CANCER RESEARCH CENTER
OF TOULOUSE – CRCT

Cancer Research Center of Toulouse – CRCT

Key figures



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, 4 of which also have CNRS accreditation, add a basic and translational research component to the IUCT–Oncopole healthcare center.

Missions

Because progress in the fight against cancer cannot be made without research, the CRCT's teams pursue four main missions:

- Carry out basic research to determine the biological mechanisms responsible for the appearance, progression and spread of cancers, and for resistance to current treatments.
- Find and develop new ways of overcoming these mechanisms and discover new anti-cancer agents.
- Design translational research projects through which the results of basic research can be transferred to clinical applications for the benefit of the IUCT–Oncopole's patients. This translational research allows the development of medical applications, especially novel approaches to diagnosis and treatment. Reciprocally, clinical data from the IUCT–Oncopole is used to reevaluate hypotheses arising from the CRCT's research projects.
- Integrate students and post-doctoral researchers into research teams so they can learn from more experienced researchers. As a complement to this experimental training, a program of seminars and other scientific events promotes dialogue and interactions between disciplines.

Research themes

The CRCT's teams focus on four basic research themes:

- Oncogenic signaling, DNA damage and genetic instability,
- RNA and cancer,
- Tumor microenvironment and metabolism,
- Onco-immunology.

And two transversal themes:

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

In addition to its research teams, the CRCT also houses a major technology cluster, which provides the cut-





ting-edge technology the site's scientists and clinicians need to explore their hypotheses and answer their research questions.

The presence of numerous clinicians in the CRCT's teams facilitates the rapid transfer of data from basic research to clinical applications and vice versa. Examples of integrated research programs include those awarded funding through the internal @IUCT-Onco-pole call for proposals.

Two new research teams joined the CRCT in 2018 and recruitment will continue in the years to come in order to further strengthen the Center's expertise.

Research programs in 2018

Restructuring Toulouse's cancer care and research offer has not only identified the different actors involved, it has also strengthened local collaborations. What is more, new collaborations are encouraged and facilitated by the provision of local funding for innovative and collaborative projects through two types of grant: one for collaborations between IUCT-Oncopole clinicians and CRCT researchers, the other for interdisciplinary projects within Toulouse's scientific community.

@IUCT-Oncopole grants for translational projects

Every year, the IUCT-Oncopole uses research-oriented donations to fund selected translational research projects. In 2018, the Fondation Toulouse Cancer Santé provided additional funding for the projects selected.

@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, which awarded funding to four projects in 2018: EPOXCAN, LUNG RESIST, ONCOPOLE and LMSTAR. The first two projects are presented below.

EPOXCAN

Characterization of the deregulation of the cholesterol metabolism in breast cancer.

Coordinators: Dr. M. Poirot and Prof. F. Dalenc

Participants: Dr. M. Poirot's, Prof. F. Dalenc's, T. Filleron's and Prof. E. Chatelut's teams

CRCT team 12's discovery of dendroginin A (DDA) revealed a new metabolic branch of the cholesterol pathway. DDA has been detected in healthy tissues in several organs, including breast tissue, but its concentration is greatly reduced in breast cancer (BC) cells. DDA's chemopreventive and anti-cancer properties make it a tumor suppressor that acts by modulating transcription factors and inhibiting the biosynthesis of OCDO, a tumor promoter which the team also identified recently. OCDO is produced in BC cells but not in healthy breast cells. This inhibition mechanism contributes to the antitumoral action of DDA. The existence of these two metabolites suggests there is a metabolic balance between them in healthy breast cells and BC cells that can either curb or stimulate the progression of BC. Characterizing this metabolic branch will allow improved stratification of BC and open the way for new therapeutic strategies targeting this pathway. EPOXCAN's first objective is to assess the proportion of BC

cells that present this metabolic deregulation. The team will then determine whether or not these metabolic deregulations are more common in certain sub-types of BC and whether they are linked to BC prognosis.

LUNG RESIST

Lung cancer: targeting early stages in the adaptive resistance to EGFR tyrosine kinase inhibitors

Coordinators: Prof. J. Mazières and Dr. O. Calvayrac

EGFR tyrosine kinase inhibitors (EGFR-TKI) are effective in patients with advanced lung cancers presenting an EGFR activating mutation, but they do not provide a cure due to the systematic appearance of resistance. Recent studies suggest that TKI resistance may be due to a population of drug-tolerant cells (DTC) which resist initially by entering a pseudo-dormant state. However, two crucial questions remain unanswered: How do these cells survive and how do they acquire the genetic alterations that enable them to recover their ability to proliferate? Targeting DTCs may provide a promising new approach for slowing the emergence of secondary resistance, but as yet not enough is known about this cell state to develop new treatments.

CRCT team 3 recently discovered that the RHOB/AKT pathway was a key EGFR-TKI resistance pathway in patients with lung cancer. Recent data suggest that the RHOB/AKT pathway may be an adaptive mechanism shared with inhibition of the ERK pathway and therefore a solid candidate for the acquisition of DTC. LUNG RESIST will use state-of-the-art technology, mouse models and patient tissue samples to comprehensively characterize the phenotypic and molecular changes associated with resistance to EGFR-TKI. This should make it possible to determine the role of the RHOB/AKT pathway in this adaptive resistance and identify possible new resistance pathways that can be targeted in order to prevent the emergence of the resistance mutations responsible for patient relapse.

Joint IUCT GIP and Fondation Toulouse Cancer Santé annual call for proposals

One of the FTCS's missions is to fund innovative, interdisciplinary and collaborative projects by the Toulouse area's medical-scientific community. Its annual call for proposals is designed 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 theme of the FTCS's 8th call for proposals, launched in 2018 in conjunction with the IUCT GIP, was "Cellular and/or molecular aspects of resistance and their potential therapeutic implications". An international scientific board awarded funding to four projects, including two involving the CRCT:1

ROADTRIP

(Resistance of pancreatic ADenocarcinoma and TRIP12) – Involvement of E3 ubiquitin ligase TRIP12 in the therapeutic resistance of pancreatic adenocarcinomas)

Coordinator: Dr. J. Torrisani

Partners: Dr. N. Duseti's (CRCM) and Dr. S. Millevoi's teams

Survival rates for pancreatic cancer remain extremely low, mainly due to the absence of specific clinical signs, early diagnostic markers and effective treatment for this cancer. As a result, pancreatic cancer is the fourth largest cause of cancer deaths. ROADTRIP's goal is to determine whether the expression of E3 ubiquitin ligase TRIP12 (Thyroid Hormone Receptor-Interacting Protein 12) can be used as a marker for predicting responses to chemotherapies for pancreatic cancer and thereby allow therapies to be targeted better. TRIP12 is a key inhibitor of the NHEJ (Non-Homologous End Joining) DNA damage repair pathway but, as the team has shown, its expression in human pancreatic adenocarcinomas is very heterogeneous. Although it is plausible that the expression of TRIP12 makes pancreatic cancer cells more sensitive to chemotherapies, the project must establish whether or not this is the case. Another of ROADTRIP's aims is to determine the molecular mechanisms that control the cellular chemosensitivity induced by TRIP12 and the mechanisms underlying the heterogeneity of expression of TRIP12 in pancreatic cancers.

MECHARESIST

Impact of mechanical constraints on therapeutic resistance: from basic research to clinical application




























Coordinator: Dr. M. Delarue

Partner: Dr. J. Guillermet-Guibert

Despite the omnipresence of mechanical constraints, studies of their effects on therapeutic strategies for treating cancer are almost non-existent. This can lead to situations where certain drugs identified *in vitro* do not undergo *in vivo* clinical tests and some that are subjected to such tests do not function. In fact, mechanical constraints can play a substantial role in drug-resistance mechanisms, during both identification and treatment. MECHARESIST's aim is to overcome this problem by designing new micro-fluid devices that can be used to determine a drug's impact under relevant mechanical conditions. The project is based on the hypothesis that mechanical constraints modulate responses to drugs in two, non-mutually exclusive ways: directly, by triggering signaling pathways specific to these constraints, and indirectly, by modifying the biophysical properties of cells (e.g., by increasing macromolecular crowding, which can dynamically reduce a drug's efficacy). This hypothesis will be tested on pancreatic cancer, which is both very aggressive and incurable, and for which Dr. Guillermet-Guibert's team at the CRCT has genetically defined mouse lines and primary cells taken from patients. Dr. Delarue's team at the LAAS-CNRS will provide cutting-edge expertise in mechanobiology. The objective is to find new mechanisms involved in resistance to chemotherapy and to develop new solutions. In terms of technological developments, the project will create a new, high-throughput screening method that will be midway between classic cell cultures and animal studies, but which should perform better than animal studies because it will use human cells.

(1) The other two projects were those presented by Didier Trouche, Director of the Integrative Biology Center and the LBCMCP, and Frédéric Lagarrigue, a researcher at the IPBS, who put forward a new theme. The FTCS's grant has enabled Dr. Lagarrigue to return to France.

Two new teams joined the CRCT in 2018,
bringing the total to 21 teams.

 01 M. Ayyoub	 05 S. Millevoi	08 S. Manenti 	12 M. Poirot / S. Silvente-Poirot 	 15 M. Bardiès	 19 F. Chibon
02 J.S. Hoffmann 	06 S. Pyronnet / C. Bousquet 	 09 J.J. Fournié		16 E. Delabesse 	 20 S. Valitutti
 03 G. Favre		10 P. Cordelier 			 21 V. Pancaldi
04 T. Levade / N. Andrieu 		 11 E. Moyal / C. Toulas	 13 H. Avet-Loiseau / L. Martinet	 17 J. Guillermet-Guibert / J.P. Delord	
 07 P. Brousset / F. Meggetto			14 E. Chatelut 	18 J.E. Sarry 	Technology cluster F. Lopez 

TEAM 1 Antitumor immunity and immunotherapy

Team leader: Prof. Maha Ayyoub

Keywords: T-lymphocyte 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

Research theme: Deciphering the molecular and cellular mechanisms involved is an essential step in overcoming tumors' resistance to immunotherapies. 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 resis-

tant 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 the development of combination therapies, in particular anticancer vaccines that can stimulate antitumor T cell responses and immune checkpoint modulators capable of reversing T cell exhaustion at the tumor site.

Major publications in 2018:

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.
2. Angeles MA, Martínez-Gómez C, Migliorelli F, Voglimacci M, Figurelli J, Motton S, Tanguy Le Gac Y, Ferron G, Martinez A. Novel Surgical Strategies in the Treatment of Gynecological Malignancies. *Curr Treat Options Oncol.* 2018 Nov 9;19(12):73.

TEAM 2 Regulation of DNA replication and genetic instability in cancers

Team accredited by the Ligue Contre le Cancer

Team leader: Dr Jean-Sébastien Hoffmann

Keywords: Replicative stress, genetic instability, therapeutic resistance

Funding sources: ANR 2016-2019, "2R-Pol" program – Coord. J.-S. Hoffmann; INCa PLBIO 2016-2019 – Coord. J.-S. Hoffmann, Ligue Contre le Cancer – Accreditation Program

Research theme: The team focuses on the mechanisms that limit replicative stress in normal cells and the consequences of replicative stress in tumor cells on genome stability. This research has identified a new replication fork regulation mechanism in which two nucleases – Artemis and XPF (Betous et al., *PLOS Genetics* 2018) – stall replication. It has also enabled the team to characterize a therapeutic resistance factor as a new prognostic biomarker in chronic lymphocytic leukemia (Grgurevic et al., *Haematologica* 2018),

and to describe a family of patients at the IUCT-Oncopole who have a germline mutation in a gene coding a replicative DNA polymerase, POLE, which plays a major role in DNA replication (Vande Perre et al., *Familial Cancer* 2018).

Major publications in 2018:

1. Bétous R, Gouillet de Rugy T, Pelegrini AL, Queille S, de Villartay JP, Hoffmann JS*. DNA replication stress triggers Rapid DNA Replication Fork Breakage by Artemis and XPF. *PLoS Genet.* 2018 14(7): e1007541.
2. Grgurevic S, Montilla-Perez P, Bradbury A, Gilhodes J, Queille S, Pelofy S, Bancaud A, Filleron T, Ysebaert L, Récher C, Laurent G, Fournié JJ, Cazaux C, Quillet-Mary A, Hoffmann JS*. DNA polymerase ϵ gene expression influences fludarabine resistance in chronic lymphocytic leukemia independently of p53 status. *Haematologica.* 2018 Jun;103(6):1038-46.
3. 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.* 2018 Oct 27.
4. Courtot L, Hoffmann JS, Valérie Bergoglio V. The Protective Role of Dormant Origins in Response to Replicative Stress. *Int J Mol Sci.* 2018 Nov 12;19(11). pii: E3569.

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 break, 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 elucidating the mechanisms involved in resistance to targeted therapies, focusing on the RTK/RAS/ERK pathway, and developing innovative biotechnologies, including split GFP and nanobodies, this research will help resolve issues in cell biology and lead to new the-

rapeutic strategies. Bioclinical (liquid biopsies) and clinical studies on lung cancers and melanoma are carried out in collaboration with the IUCT.

Major publications in 2018:

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*. 2018 Dec 27. pii: 201810409.
2. Garassino MC, Cho BC, Kim JH, Mazières J, Vansteenkiste J, Lena H, Corral Jaime J, Gray JE, Powderly J, Chouaid C, Bidoli P, Wheatley-Price P, Park K, Soo RA, Huang Y, Wadsworth C, Dennis PA, Rizvi NA; ATLANTIC Investigators. Durvalumab as third-line or later treatment for advanced non-small-cell lung cancer (ATLANTIC): an open-label, single-arm, phase 2 study. *Lancet Oncol*. 2018 Apr;19(4):521-36.
3. Calvayrac O, Nowosad A, Cabantous S, Lin LP, Figarol S, Jeannot P, Serres M, Callot C, Percey 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*. 2018 Dec 11.
4. Koraichi F, Gence R, Bouchenot C, Grosjean S, Lajoie-Mazenc I, Favre G, Cabantous S. High-content tripartite split-GFP cell-based assays to screen for modulators of small GTPase activation. *J Cell Sci*. 2018 Jan 8;131(1).
5. Tichauer RH, Favre G, Cabantous S, Landa G, Hemeryck A, Brut M. Water Distribution within Wild-Type NRas Protein and Q61 Mutants during Unrestrained QM/MM Dynamics. *Biophys J*. 2018 Oct 16;115(8):1417-30.

TEAM 4 Spingolipid metabolism, cell death and tumor progression

Team accredited by the Ligue Contre le Cancer (2013-2018)

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

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-Oncopole, Société Française de Dermatologie, 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 ASAHI is associated with invasive phenotype in melanomas via the integrin alpha-V beta5/FAK signaling pathway.
- Several alterations to ceramide metabolism contribute to the resistance of melanomas to BRAF inhibitors.

Major publications in 2018:

1. Pérés M, Montfort A, Andrieu-Abadie N, Colacios C, Ségui B. SIP: the elixir of life for naive T cells. *Cell Mol Immunol*. 2018 Jul;15(7):657-9.
2. Dalmau N, Andrieu-Abadie N, Tauler R, Bedia C. Phenotypic and lipidomic characterization of primary human epidermal keratinocytes exposed to simulated solar UV radiation. *J Dermatol Sci*. 2018 Oct;92(1):97-105.
3. Garandeau D, Noujarède J, Leclerc J, Imbert C, Garcia V, Bats ML, Rambow F, Gilhodes J, Filleron T, Meyer N, Brayer S, Arcucci S, Tartare-Deckert S, Ségui B, Marine JC, Levade T, Bertolotto C, Andrieu-Abadie N. Targeting the Sphingosine 1-Phosphate Axis Exerts Potent Antitumor Activity in BRAFi-Resistant Melanomas. *Mol Cancer Ther*. Epub 2018 Nov 27.

4. 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 J](#), Ballotti R, [Andrieu-Abadie N](#), Bertolotto C. Lysosomal acid ceramidase ASAH1 controls the transition between invasive and proliferative phenotype in melanoma cells. **Oncogene**. Epub

2018 Sep 25.

5. Use of sphingosine kinase 1 as biomarker for predicting response to immune-checkpoint inhibitors. **EP18305178**.

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

Team leader: Dr. Stefania Millevoi

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

Funding sources: ANR, Cancéropôle GSO, IRSC

Research theme: The team's aim is to determine the role of RNA binding proteins (RBPs) in cancer cells in order to understand the reprogramming of genome expression and to decipher how RNA-protein networks are modulated by oncogenic signaling and DNA damage. Results of the team's basic research can be applied to translational research projects into glioblastoma resistance to chemo-radiotherapy. In addition, research carried out in collaboration with CRCT team 9, led by J.-J. Fournié, has highlighted the importance of RBPs in the post-transcriptional coordination of antitumor immune responses. These results have opened new

horizons for developing new classes of immunotherapy drugs targeting immune checkpoints. In 2018, Anouchka Modesto, an IUCT-Oncopole radiation oncologist, was invited to join the team to lead a new research program on head and neck cancers (HNSCC). In another noteworthy event, the Association de Recherche Contre le Cancer (ARC) awarded its Hélène Starck prize to Marie Cargnello for her post-doctoral project on mTOR oncogenic signaling and the regulation of protein synthesis (funded by the ARC and Cancéropôle GSO).

Major publications in 2018:

1. Franchini DM, Lanvin O, Tosolini M, Patras de Campaigno E, Cammas A, Péricart S, Scarlata CM, Lebras M, Rossi C, Ligat L, Pont E, Arimondo PB, Laurent C, Ayyoub M, Despas F, Lapeyre-Mestre M, [Millevoi S*](#), [Fournié J*](#). Microtubule-driven stress granule dynamics regulates inhibitory immune checkpoints expression in T cells. **Cell Rep**. 2018. doi: 10.1016/j.celrep.2018.12.014.
2. Franchini DM, Lanvin O, [Millevoi S](#), [Fournié JJ](#). Use of inhibitors of stress granule formation for targeting the regulation of immune response. **Brevet EP18306286.8**, 2018.

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 (AML)

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 how protein

synthesis and secretion are involved in pancreatic cancers and acute myeloid leukemia (AML), and whether these processes can be targeted for therapeutic intervention. Its 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. These studies have revealed the importance of tumor microenvironment heterogeneity and the value of using the antisecretory

action of somatostatin analogues to target its pro-tumor activity.

Major publications in 2018:

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*. 2018 Dec 21.

2. Günther T, Tulipano G, Dournaud P, Bousquet C, Csaba Z, Kreienkamp HJ, Lupp A, Korbonits M, Castaño JP, Wester HJ, Culler M, Melmed S, Schulz S. International Union of Basic and Clinical Pharmacology. CV. Somatostatin Receptors: Structure, Function, Ligands, and New Nomenclature. *Pharmacol Rev*. 2018 70:763–835.

3. Ogier C, Colombo PE, Bousquet C, Canterel-Thouennon L, Sicard P, Garambois V, Thomas G, Gaborit N, Jarlier M, Pirot N, Pugnière M, Vie N, Gongora C, Martineau P, Robert B, Pèlerin A, Chardès T, Larbouret C. Targeting the NRG1/HER3 pathway in tumor cells and cancer-associated fibroblasts with an anti-neuregulin 1 antibody inhibits tumor growth in pre-clinical models of pancreatic cancer. *Cancer Lett*. 2018 432:227–36.

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 pour la Recherche sur le Cancer, Fondation pour la Recherche Médicale, Association Laurette Fugain, Institut CALYM, Fondation Fonroga.

Research theme: The team's research focuses on the role non-coding RNA (ncRNA) plays in regulating the cell pathways involved in the development and progression of cancer. Its goals are to determine the physiological and pathological roles played by these ncRNAs, ascertain the impact of their deregulation on prognosis, tumor progression and responses to treatment, and elucidate the upstream mechanisms of ncRNA regulation. To this end, it is currently 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.

Major publications in 2018:

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*. 2018 Sep 27. pii: haematol.2018.195131.

2. Congras A, Caillet N, Torossian N, Quelen C, Brousset P, Lamant L, Meggetto F*, Hoareau-Aveilla C. Doxorubicin-induced loss of DNA topoisomerase II and DNMT1-dependent suppression of MiR-125b induces chemoresistance in ALK-positive cells. *Oncotarget*. 2018. 8;9(18):14539–51. *corresponding author

3. Jamrog L, Chemin G, Fregona V, Coster L, Pasquet M, Oudinet C, Rouquié N, Prade N, Lagarde S, Cresson C, Hébrard S, Nguyen Huu NS, Bousquet M, Quelen C, Brousset P, Mancini SJC, Delabesse E, Khamlichi AA, Gerby B, Broccardo C. PAX5-ELN oncoprotein promotes multistep B-cell acute lymphoblastic leukemia in mice. *Proc Natl Acad Sci USA*. 2018. 9;115(41):10357–62.

4. Laurent C, Haïoun C, Brousset P, Gaulard P. New insights into breast implant-associated anaplastic large cell lymphoma. *Curr Opin Oncol*. 2018 Sep;30(5):292–300.

5. Perron E, Pissaloux D, Charon Barra C, Karanian M, Lamant L, Parfait S, Alberti L, de la Fouchardière A. Melanocytic Myxoid Spindle Cell Tumor With ALK Rearrangement (MMySTAR): Report of 4 cases of a nevus variant with potential diagnostic challenge. *Am J Surg Pathol*. 2018 May;42(5):595–603.

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, Cancéro-

pôle 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 players 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. Greater knowledge of how players in the cell cycle and autophagy impact these cancer cells' responses and resistance to therapeutic agents will enable researchers to identify new therapeutic targets. The team has revealed the roles played by the transcription factor ATF4 in inducing autophagy, by CHK1 and Pim2 in mitosis, by CHK1 as a prognostic factor and therapeutic target, and by ubiquitin-specific protease-7 (USP7) as a CHK1 regulator and therapeutic target in AML.

Major publications in 2018:

- Heydt Q, Larrue C, Saland E, Sarry JE, Besson A, Manenti S, Joffre C*, Mansat-De Mas V*. Oncogenic FLT3-ITD supports autophagy via ATF4 in acute myeloid leukemia. *Oncogene*. 2018 Feb 8, 37: 787-97 (*equal participation, co-corresponding authors)
- Adam K†, Cartel M†, Lambert M†, David L, Yuan L, Besson A, Mayeux P*, Manenti S*, Didier C*. A PIM2-CHK1 signaling pathway regulates PLK1 phosphorylation and functions during mitosis. *J Cell Science*. 2018, Aug 10;131(15).
- Perchey R, Serres M, Nowosad A, Creff J, Callot C, Gay A, Manenti S, Margolis R, Hatzoglou A, Besson A. p27Kip1 regulates the microtubule bundling activity of PRC1. *BBA- Molecular Cell research*. 2018, 1865 (11A) :1630-9
- 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 Pathology*. 2018 Sep 11.
- Brevet : Use of USP7 inhibitors for the treatment of acute myeloid leukemia BIO18527 – MANENTI / MC. Dépôt N° EPI9305181.0

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 pour la Recherche sur le Cancer, Fondation Toulouse Cancer Santé, POCTEFA, imCore Roche

Research theme: The team's aim is to improve the efficacy of treatments for non-Hodgkin B lymphoma (NHL) in order to prevent relapses and overcome unresponsiveness to current treatments. This work includes developing new molecular and cellular analysis tools and new biological models that can be used to determine ways of targeting NHL. The team also explores potential targets and uses preclinical models to test new molecules before subjecting them to phase I and II clinical trials at the IUCT-Oncopole.

Major publications in 2018:

- Pericart S, Tosolini M, Gravelle P, Rossi C, Traverse-Glehen A, Amara N, Franquet C, Martin E, Bezombes C, Laurent G, Brousset P, Fournié JJ, Laurent C. Profiling Immune Escape in Hodgkin's and Diffuse large B-Cell Lymphomas Using the Transcriptome and Immunostaining. *Cancers* (Basel) 2018 Oct 31;10(11)
- Gravelle P, Pericart S, Tosolini M, Fabiani B, Coppo P, Amara N, Traverse-Glehen A, Van Acker N, Brousset P, Fournié JJ, Laurent C. EBV infection determines the immune hallmarks of plasmablastic lymphoma. *Oncimmunology* 2018. Dec 17;8(3):1554175.
- Grgurevic S, Montilla-Perez P, Bradbury A, Gilhodes J, Queille S, Pelofy S, Bancaud A, Filleron T, Ysebaert L, Récher C, Laurent G, Fournié JJ, Cazaux C, Quillet-Mary A, Hoffmann JS. NA polymerase γ gene expression influences fludarabine resistance in chronic lymphocytic leukemia independently from p53 status. *Hematologica*. 2018 Jun;103(6):1038-46.
- Le Roy A, Prébet T, Castellano R, Goubard A, Riccardi F, Fauriat C, Granjeaud S, Benyamine A, Castanier C, Orlanducci F, Ben Amara A, Pont F, Fournié JJ, Collette Y, Mege JL, Vey N, Olive D. Immunomodulatory Drugs Exert Anti-Leukemia Effects in Acute Myeloid Leukemia by Direct and Immunostimulatory Activities. *Front Immunol*. 2018 May 4;9:977.
- Ghez D, Calleja A, Pratin C, Baron M, Ledoux MP, Damaj G, Dupont M, Dreyfus B, Ferrant E, Herbaux C, Laribi K, Le Calloch R, Malphettes M, Paul F, Souchet L, Truchan-Graczyk M, Delavigne K, Dartigeas C, Ysebaert L. Early-onset invasive aspergillosis and other fungal infections in patients treated with ibritinib. *Blood*. 2018 Apr 26;131(17):1955-9.

TEAM 10 Molecular heterogeneity of pancreatic tumors

Team leader: Dr. Pierre Cordelier

Keywords: Pancreatic cancer, therapeutic resistance,

oncolytic viruses, biomarkers, nanotechnologies

Funding sources: Ligue Contre le Cancer, ImCore Genentech, Fondation Toulouse Cancer Santé, RHU

PIR2, Occitanie Regional Council, Inserm

Research theme: Despite the relatively low incidence of pancreatic adenocarcinoma, 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 around the world by 2030.

The team's goal is to determine the molecular bases underlying pancreatic tumors' resistance to current therapies, most notably innovative biotherapies and especially oncolytic therapies, and to develop new

technological approaches to improve the treatments available to patients.

Major publications in 2018:

1. [Cordelier P.](#) Keep Quiet and Stay in Line! Smart Polymers to Keep an Eye on Pancreatic Tumors. *Mol Ther.* 2018 Apr 4;26(4):940-1.
2. [Cachoux J.](#) Brut M, Bancaud A, [Cordelier P.](#) Leïchlé T. Spatial Analysis of Nanofluorescence-Embedded Biosensors for Wash-Free Single-Nucleotide Difference Discrimination. *ACS Sens.* 2018 Mar 23;3(3):606-11.
3. Canivet C, Gourgou-Bourgade S, Napoléon B, Palazzo L, Flori N, Guibert P, Piesen G, Farges-Bancel D, Seitz JF, Assenat E, Vendrely V, Truant S, Vanbiervliet G, Berthelémy P, Garcia S, [Gomez-Brouchet A.](#) [Buscaïl L.](#) [Bournet B.](#) BACAP Consortium. A prospective clinical and biological database for pancreatic adenocarcinoma: the

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: INCa, Inserm, ARC, Ligue Contre le Cancer, ARTC, PHUC CAPTOR, Incyte, AstraZeneca

Research theme: The team's objective is to optimize radiotherapy-based treatments for glioblastoma (GBM). In order to help achieve this goal, it has set up a national research project (MoGlimaging) to study GBM heterogeneity and model therapeutic resistance mechanisms. This project combines three lines of research: i) intrinsic radioresistance, including the role of integrins and FGFR pathways; ii) induced radioresistance via GBM stem cell plasticity; and iii) mechanisms involving DNA repair genes. The results of this translational research are transferred to early phase clinical trials, designed and carried out in the radiotherapy department at the IUCT-OncoPole, associated with metabolic imaging studies. These trials are used to test potential targets that have been identified and partly confirmed (in partnership with drug companies) via specific inhibition by pharmacological inhibitors.

Furthermore, the IUCT-OncoPole's radiotherapy department is running several clinical trials of combined radiotherapy-immunotherapy treatments aimed at optimizing radiotherapy's effectiveness in treating a wide variety of tumors, especially GBM, cerebral metastases, and head and neck cancers. Ancillary biological and imaging studies, carried out in conjunction with CRCT team 1 and other French research teams specializing in imaging, provide data on response profiles to these combinations.

Major publications in 2018:

1. [Massabeau C.](#) [Khalifa J.](#) [Filleron T.](#) [Modesto A.](#) [Bigay-Gamé L.](#) [Plat G.](#) [Dierickx L.](#) [Aziza R.](#) [Rouquette J.](#) [Gomez-Roca C.](#) [Mounier M.](#) [Delord JP.](#) [Toulas C.](#) [Olivier P.](#) [Chatelut E.](#) [Mazières J.](#) [Cohen-Jonathan Moyal E.](#) Continuous infusion of Cilengitide plus chemoradiotherapy for patients with stage III non-small cell lung cancer: a phase I study. *Clin Lung Cancer.* 2018 May; 19(3):e277-e285
2. [Attal J.](#) [Chaltiel L.](#) [Lubrano V.](#) [Sol JC.](#) [Lanaspeze C.](#) [Vieillevisne L.](#) [Latorzeff I.](#) [Cohen-Jonathan Moyal E.](#) Subventricular zone involvement at recurrence is a strong predictive factor of outcome following high grade glioma reirradiation. *J Neurooncol.* 2018; 6(2):413-9.
3. [Rudà R.](#) [Reifenberger G.](#) [Frappaz D.](#) [Pfister SM.](#) [Laprie A.](#) [Santarius T.](#) [Roth P.](#) [Tonn JG.](#) [Soffietti R.](#) [Weller M.](#) [Cohen-Jonathan Moyal E.](#) EANO guidelines for the diagnosis and treatment of ependymal tumors. *Neuro-Oncol.* 2018; 20(4):445-56
4. [Kowalski-Chauvel A.](#) [Modesto A.](#) [Gouaze-Andersson V.](#) [Baricault L.](#) [Gilhodes J.](#) [Delmas C.](#) [Lemarie A.](#) [Toulas C.](#) [Cohen-Jonathan Moyal E.](#) [Seva C.](#) Alpha-6 integrin promotes radio-resistance of glioblastoma by modulating DNA damage response and the transcription factor ZEB1. *Cell Death & Dis.* 2018 Aug 29;9(9):872
5. [Malric L.](#) [Monferran S.](#) [Delmas C.](#) [Arnauduc F.](#) [Dahan P.](#) [Boyrrie 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.* 2018 Sep 28.*Co-last authors

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: IdEx, INCa (PRTK, PLBIO), Fondation Toulouse Cancer Santé, Ligue Contre le Cancer, DFG

Research theme: The team's research into deregulations in the cholesterol metabolism 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 obtain a better understanding of the mechanisms underlying both acquired and intrinsic resistance to conventional treatments.

Major publications in 2018:

1. [Silvente-Poirot S, Dalenc F, Poirot M](#). The effects of cholesterol-derived oncometabolites on nuclear receptor function in cancer. **Cancer Res.** 2018; 78(17): 4803-8
2. [Record M, Silvente-Poirot S, Poirot M, Wakelam M](#). Extracellular vesicles: lipids as key components of their biogenesis and functions. **J Lipid Res.** 2018. 59(8):1316-24.
3. [Poirot M, Soules R, Mallinger A, Dalenc F, Silvente-Poirot S](#). Chemistry, biochemistry, metabolic fate and mechanism of action of 6-oxo-cholestan-3 β ,5 α -diol (OCDO), a tumor promoter and cholesterol metabolite. **Biochimie.** 2018; 153c:138-48.
4. [Poirot M, Silvente-Poirot S](#). The tumor-suppressor cholesterol metabolite, dendrogenin A, is a new class of LXR modulator activating lethal autophagy in cancers. **Biochem. Pharmacol.** 2028; 153, 75-81
5. [Silvente-Poirot S, Segala G, Poirot MC, Poirot M](#). Ligand-dependent transcriptional induction of lethal autophagy: a new perspective for cancer treatment. **Autophagy.** 2018; 14(3):555-7.
6. [Khallouki F, Owen RW, Silvente-Poirot S, Poirot M](#). Bryonolic acid blocks cancer cell clonogenicity and invasiveness through the inhibition of fatty acid:cholesteryl esters formation. **Biomedicines.** 2018; 21 Feb 12;6(1).

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 pour la Recherche sur le Cancer, 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:

- Carry out large-scale genome sequencing of tumors in order to identify groups of patients who are likely

to respond to different treatments and thereby help clinicians in their therapeutic choices.

- Characterize MM patients' immune systems in order to activate these systems to eliminate tumor cells.
- Analyze interactions between tumor cells and normal bone marrow cells, in particular mesenchymal stem cells.

Major publications in 2018:

1. [Samur MK, Minvielle S, Gulla A, Fulcinitti M, Cleyne A, Aktas Samur A, Szalat R, Shammas M, Magrangeas F, Tai YT, Auclair D, Keats J, Richardson P, Attal M, Moreau P, Anderson KC, Parmigiani G, Avet-Loiseau H*](#). Long intergenic non-coding RNAs have an independent impact on survival in multiple myeloma. **Leukemia.** 2018 Dec;32(12):2626-35.
2. [Nakamura K, Kassem S, Cleyne A, Chrétien ML, Guillerey C, Putz EM, Bald T, Förster I, Vuckovic S, Hill GR, Masters SL, Chesi M, Bergsagel PL, Avet-Loiseau H, Martinet L*, Smyth MJ*](#). Dysregulated IL-18 Is a Key Driver of Immunosuppression and a Possible Therapeutic Target in the Multiple Myeloma Microenvironment. **Cancer Cell.** 2018 Apr 9;33(4):634-48
3. [Guillerey C, Harjunpää H, Carrié N, Kassem S, Teo T, Miles K, Krumeich S, Weu-](#)

lerse M, Cuisinier M, Stannard K, Yu Y, Minnie SA, Hill GR, Dougall WC, Avet-Loiseau H, Teng MWL, Nakamura K, Martinet L, Smyth MJ. TIGIT immune checkpoint blockade restores CD8+ T-cell immunity against multiple myeloma. **Blood**. 2018 Oct 18;132(16):1689–94.

4. Michallet M, Chapuis-Cellier C, Dejoie T, Lombard C, Caillon H, Sobh M, Moreau

P, Attal M, Avet-Loiseau H. Heavy+light chain monitoring correlates with clinical outcome in multiple myeloma patients. **Leukemia**. 2018 Feb;32(2):376–82.

5. Cleyne A, Samur M, Perrot A, Buisson L, Maheo S, Fulciniti M, Attal M, Munshi N, Avet-Loiseau H, Corre J. Variable BCL2/BCL2L1 ratio in multiple myeloma with t(11;14). **Blood**. 2018 Dec 27;132(26):2778–80.

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 (PK–PD) relationships, pharmacogenetics, metabolism

Funding sources: PHRC, ANSM, ITMO Cancer

Research theme: The team carries out translational and clinical research to drive the dose individualization of anticancer drugs. Its work mostly involves identifying inter-individual variability in pharmacokinetics and pharmacogenetics that can be used to adapt treatment to each patient and thereby increase the efficacy of drug doses while reducing their toxicity. Several studies based on the nonlinear mixed effects approach are ongoing. The purpose of these studies is to:

- Monitor the effects of drugs in order to adjust doses during a protocol;

- Determine how drugs are metabolized in order to assess their hepatotoxicity and potential side effects; Investigate the deregulation of the cholesterol metabolism in breast cancers described by CRCT team 12;
- Use pharmacokinetic–pharmacodynamic modeling to quantify the effects of different treatments.

Major publications in 2018:

1. Paludetto MN, Bijani C, Puisset F, Bernardes-Génisson V, Arellano C, Robert A. Metalloporphyrin-Catalyzed Oxidation of Sunitinib and Pazopanib, Two Anti-cancer Tyrosine Kinase Inhibitors: Evidence for New Potentially Toxic Metabolites. **J Med Chem**. 2018; 61:7849–60.

2. White-Koning M, Osborne C, Paci A, Boddy AV, Chatelut E, Veal GJ. Investigating the potential impact of dose banding for systemic anti-cancer therapy in the paediatric setting based on pharmacokinetic evidence. **Eur J Cancer**. 2018 Jan 12;91:56–67.

3. Thomas F, Veal GJ, El Balkhi S, Lafont T, Picard N, Brugieres L, Chatelut E, Piguet C. Therapeutic drug monitoring and dose adaptation of cisplatin in a newborn with hepatoblastoma: a case report. **Cancer Chemother Pharmacol**. 2018;82:361–5

4. Paludetto MN, Puisset F, Le Louedec F, Allal B, Lafont T, Chatelut E, Arellano C. Simultaneous monitoring of pazopanib and its metabolites by UPLC-MS/MS. **J Pharm Biomed Anal**. 2018 May 30;154:373–83.

5. Chatelut E, Bruno R, Ratain MJ. Intraindividual Pharmacokinetic Variability: Focus on Small-Molecule Kinase Inhibitors. **Clin Pharmacol Ther**. 2018;103:956–8.

TEAM 15 Multiscale dosimetry for radiotherapy optimization

Team leader: Dr. Manuel Bardiès

Keywords: Dosimetry, Monte-Carlo modeling, therapy optimization

Funding sources: IAEA, 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 three main projects:

- Dositest 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 and EuraMET),

- OpenDose aims to generate dosimetric reference data for molecular radiotherapy (17 partners),
- STEREPID was set up to study in vivo dosimetry in external radiotherapy.

Major publications in 2018:

1. Santoro L, Mora-Ramirez E, Trauchessec D, Chouaf S, Eustache P, Pouget JP, Kotzki PO, Bardiès M, Deshayes E. Implementation of patient dosimetry in the clinical practice after targeted radiotherapy using [177Lu]-[DOTA0, Tyr3]-octreotate.

EJNMMI Res. 2018 8(1):103.

2. Taïeb D, Foletti JM, [Bardiès M](#), Rocchi P, Hicks RJ, Haberkorn U. PSMA-Targeted Radionuclide Therapy. **J Nucl Med** 2018 59(5):747-8.

3. Flux GD, Sjogreen Gleisner K, Chiesa C, Lassmann M, Chouin N, Gear J, [Bardiès M](#), Walrand S, Bacher K, Eberlein U, Ljungberg M, Strigari L, Visser E, Konijnenberg MW. From fixed activities to personalized treatments in radionuclide therapy: lost in translation? **Eur J Nucl Med Mol Imaging**. 2018 45(1):152-4.

4. Incerti S, Kyriakou I, Bernal MA, [Bordage MC](#), Francis Z, Guatelli S, Ivanchenko

V, Karamitros M, Lampe N, Lee SB, Meylan S, Min CH, Shin WG, Nieminen P, Sakata D, Tang N, Villagrana C, Tran HN, Brown JMC. Geant4-DNA example applications for track structure simulations in liquid water: A report from the Geant4-DNA Project. **Med Phys**. 2018 Jun 14.

5. [Attal J](#), [Chattiel L](#), Lubrano V, Sol JC, [Lanaspeze C](#), [Viellevigne L](#), Latorzeff I, [Cohen-Jonathan Moyal E](#). Subventricular zone involvement at recurrence is a strong predictive factor of outcome following high grade glioma reirradiation. **J Neuro Oncol**. 2018 Jan;136(2):413-9.

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, ARC, Occitanie Regional Council, Association Laurette Fugain, Société Française des Cancers de l'Enfant, 111 des Arts, Association Cassandra

Research theme: Hematopoiesis, the process by which all types of blood cells are produced, is finely regulated, notably by transcription factors (TF). Deregulation of hematopoiesis at an early stage can lead to acute leukemia (AL), defined as the early blockade of differentiation and the uncontrolled proliferation of blasts. The team's work, which lies at the interface between clinical and basic research, aims not just to improve diagnosis, but also to develop alternative therapies by identifying genomic alterations in transcription fac-

tors (TF) in AL patients and then determining the role of these alterations in the leukemia process by modeling them in mouse models.

Having recently identified recurrent mutations in AL patients that involve two TFs, PAX5 and GATA2, the team is currently using experimental mouse models expressing these mutations to study transformation and relapse mechanisms.

Major publications in 2018:

1. [Jamrog L](#), Chemin G, [Fregona V](#), [Coster L](#), [Pasquet M](#), Oudinet C, [Rouquié N](#), [Prade N](#), [Lagarde S](#), [Cresson C](#), [Hébrard S](#), Nguyen Huu NS, [Bousquet M](#), [Quelen C](#), [Brousset P](#), Mancini SJ, [Delabesse E](#), Khamlichi AA, [Gerby B](#), [Broccardo C](#). PAX5-ELN oncoprotein promotes multistep B-cell acute lymphoblastic leukemia in mice. **Proc Natl Acad Sci USA**. 2018 Oct 9;115(41):10357-62.

2. [Cresson C](#), Péron S, [Jamrog L](#), [Rouquié N](#), [Prade N](#), [Dubois M](#), [Hébrard S](#), [Lagarde S](#), [Gerby B](#), Mancini SJ, [Cogné M](#), [Delabesse E](#), [Delpy L](#), [Broccardo C](#). PAX5A and PAX5B isoforms are both efficient to drive B cell differentiation. **Oncotarget**. 2018 Aug 28;9(67):32841-54.

TEAM 17 SIGDYN-P13K isoforms, signaling and cancerogenesis

Team leaders: Dr. Julie Guillermet-Guilbert and Prof. Jean-Pierre Delord

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

P13K plays a central role in cell proliferation, survival, differentiation, migration and metabolism. P13K class 1 is a family of four enzymes with non-redundant functions. P13K 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 P13K in order to offer patients effective new therapeutic combinations. Phase I and phase II trials have tested both pan-P13K and isoform-specific P13K inhibitors, but their use is difficult. Specific inhibitors are more promising and

should enable advanced solid tumors to be treated.

Major publications in 2018:

1. [Le Naour A, Mevel R, Thibault B, Courtais E, Chantalat E, Delord JP, Couderc B, Guillermet-Guibert J, Martinez A.](#) Effect of combined inhibition of p110 alpha PI3K isoform and STAT3 pathway in ovarian cancer platinum-based resistance. **Oncotarget.** 2018 Jun 5;9(43):27220–32. eCollection 2018 Jun 5.

2. [Cintas C, Douché T, Therville N, Arcucci S, Ramos-Delgado F, Basset C, Thibault B, Guillermet-Guibert J.](#) Signal-Targeted Therapies and Resistance Mechanisms in Pancreatic Cancer: Future Developments Reside in Proteomics.. **Cancers** (Basel). 2018 Jun 1;10(6). pii: E174.

3. [Cintas C, Guillermet-Guibert J.](#) Heterogeneity of Phosphatidylinositol-3-Kinase (PI3K)/AKT/Mammalian Target of Rapamycin Activation in Cancer: Is PI3K Isoform Specificity Important? **Front Oncol.** 2018 Jan 22;7:330. eCollection 2017

TEAM 18 RESIST@ML

Drug resistance and oncometabolism in acute myeloid leukemia (AML)

Team accredited by the Ligue Contre le Cancer

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 and spleen ecosystem

Funding sources: Ligue Contre le Cancer, PIA-PSPC IMODI, LabEx TOUCAN, PHUC CAPTOR

Research theme: The team's goal is to understand and target the metabolic mechanisms responsible for therapeutic resistance in AML. A combination of metabolomic, transcriptomic, pharmacological and functional approaches are being used in conjunction with xenograft models and samples from patients to investigate the roles played in resistance mechanisms by mitochondrial energy production and metabolic flexibility, by interactions between leukemic blasts and stromal cells, and by potential regulators of metabolic and energy pathways. This research has already shown that AML cells resistant to AraC have a "HIGH OxPHOS" gene signature, dependent on FA oxidation, and overexpress the CD36 FA transporter. A prelini-

cal xenograft model drawn up by the team is now being used to predict responses to AraC (and other targeted therapies) in mice and patients, characterize chemoresistance, identify new therapeutic targets and predict patient relapse. The results will help clinicians determine the most appropriate therapy for patients.

Major publications in 2018:

1. [Stuani L, Riols F, Millard P, Sabatier M, Batut A, Saland E, Viars F, Tonini L, Zaghdoudi S, Linares LK, Portais JC, Sarry JE, Bertrand-Michel J.](#) Stable Isotope Labeling Highlights Enhanced Fatty Acid and Lipid Metabolism in Human Acute Myeloid Leukemia. **Int. J. Mol. Sci.** 2018 Oct 25;19(11).

2. [Bertoli S, Paubelle E, Bérard E, Saland E, Thomas X, Tavitian S, Larcher MV, Vergez F, 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.** Epub 2018 Nov 28.

3. [Bertoli S, Picard M, Bérard E, Griessinger E, Larrue C, Mouchel PL, Vergez F, Tavitian S, Yon E, Ruiz J, Delabesse E, Luquet J, Linares LK, Saland E, Carroll M, Danet-Desnoyers G, Sarry A, Huguet F, Sarry JE, Récher C.](#) Dexamethasone in hyperleukocytic acute myeloid leukemia. **Haematologica.** 2018 Jun;103(6):988–98.

4. [Baik H, Boulanger M, Hosseini M, Kowalczyk J, Zaghdoudi S, Salem T, Sarry JE, Hicheri Y, Cartron G, Piechaczyk M, Bossis G.](#) Targeting the SUMO pathway primes all-trans retinoic acid-induced differentiation of non-promyelocytic acute myeloid leukemias. **Cancer Res.** 2018 May 15;78(10):2601–13.

5. Dépôt de brevet européen (Nov. 2018) « Methods and pharmaceutical compositions for the treatment of acute myeloid leukemia by eradicating leukemic stem cells » : CALCRL.

6. Dépôt de brevet européen (Nov. 2018) « Methods and pharmaceutical compositions for the treatment of acute myeloid leukemia by eradicating residual cells » : MPO.

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 pour la Recherche sur le Cancer, Fondation pour la Recherche Médicale, Liddy Shriver Sarcoma Initiative

Research theme: The team's objective is to understand the chromosomal mechanisms underlying the oncogenesis of pleomorphic sarcomas, which are characterized by high chromosomal instability. Its work has already identified some important players in this oncogenesis (MDM2, CDK4, TP53, RB1, MYOCD1) and linked the tumors' aggressiveness to this chromosomal instability. However, the main drivers of this instability have not yet been identified. In order to more fully understand these oncogenesis mechanisms, the team is currently focusing on two aspects of pleomorphic sarcomas: i) Genome alterations, via an exhaustive study conducted using whole genome and transcriptome sequencing approaches; ii) Cellular mechanisms, in particular, the tumor-cell fusion the team has observed in these tumors.

Because the ultimate aim is to improve treatment for patients, research is also being done to develop tools to improve diagnosis and monitor the evolution of

patients. Having previously identified and validated an almost universal prognostic expression signature in sarcomas, the team is currently working on turning this signature into a practical tool for patient care. Two major grants awarded by the INCa in 2018 have 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).

Major publications in 2018:

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 CIN-SARC Performances. *Ann. Oncol.* Oct 18, 2018.
2. Le Guellec S, Lesluyes T, Sarot E, Valle C, Filleron T, Rochaix P, Valentin T, Pérot G, Coindre JM, Chibon F. Validation of the Complexity INDEX in SARCOMAS Prognostic Signature on Formalin-Fixed, Paraffin-Embedded, Soft-Tissue Sarcomas. *Ann. Oncol.* 2018 Aug 1;29(8):1828-35
3. 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.* Oct 2018.
4. Hemming, ML, Lawlor MA, Zeid R, Lesluyes T, Fletcher JA, Raut CP, Sicinska ET, Chibon F, Armstrong SA, Demetri GD, Bradner JE. Gastrointestinal Stromal Tumor Enhancers Support a Transcription Factor Network Predictive of Clinical Outcome. *Proc Natl Acad Sci USA.* 2018 Jun 19;115(25):E5746-E5755.
5. Chibon F, Lesluyes T, Valentin T, Le Guellec S. CINSARC signature as a prognostic marker for clinical outcome in sarcomas and beyond. *Genes, Chromosomes Cancer,* Nov 1, 2018.

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 Contre le Cancer, ANR: LabEx TOUCAN, Occitanie Regional Council, Cancéropôle

GSO, Fondation Toulouse Cancer Santé, F. Hoffmann-La Roche, Laboratoires Pierre Fabre

Research theme: The team is known for its expertise in using state-of-the-art imaging techniques to dissect the human t-cell activation and regulation mechanisms that occur at immunological synapses. Its research on the lytic synapses that form between cytotoxic human t-cells (CTL) and cancer cells has helped highlight

the idea that lytic synapses are the sites where CTL cytotoxic mechanisms are triggered and rapidly executed, and where tumor cells' first defense strategies are deployed. An important aspect of this work is the long-standing collaboration with mathematicians and computer scientists, which includes supervising collaborators and publishing the results of mathematical modeling of the CTL/tumor cell confrontation. Although the team focuses entirely on human T-cells, it has extended its research to cover the biology of human mastocytes, as well as interactions between mastocytes and T-cells in inflammation and cancer. In March 2018, the team moved to the CRCT where it has established a strong network of collaborations with patho-

logists, pharmacologists and clinicians working in the field of tumor immunology.

Major publications in 2018:

1. Gonnard 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.
2. Espinosa E, Valitutti S, Laroche M, Laurent C, Apoil PA, Hermine O, Lavit M, Paul C, Bulai Lividenau C. Hydroxychloroquine as a novel therapeutic approach in mast cell activation disease. **Clin Immunol**. 2018; 194, 75.
3. Abreu A, Frenois FX, Valitutti S, Brousset P, Deneffe P, Naegel B, Wenmert C. Model-based graph segmentation in 2-D fluorescence microscopy images. **IEEEXPlore**, International conference proceedings. International Conference on Pattern Recognition, Beijing, China (2018). Extended article with figures and results.
4. Espinosa E, Valitutti S. New roles and controls of mast cells. **Curr Opin Immunol**. 2018; 50,39. Review
5. Filed patent : Filali L, Müller S, Puissegur MP and Valitutti S. Methods and kit for assaying lytic potential of immune effector cells (ref. BIO18284 VALITUTTI) EP 18 306 576.2 filed on Nov 28, 2018.

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 and Inserm)

Research theme: The team's research focuses on applying bioinformatics methods to oncoimmunology in order to improve understanding of how variability in patient profiles (transcriptome and characteristics of immune cells) impacts responses to treatment, including but not limited to immunotherapy approaches. 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 different 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 the interactions between different types of cells in the tumor microenvironment, particularly in pancreatic adenocarcinomas. This will enable the team to go beyond quantifying different types of cells to perform *in-silico* simulations of the tumor microenvironment.

Major publications in 2018:

1. Ecker S, Pancaldi V, Valencia A, Beck S, Paul DS. Epigenetic and Transcriptional Variability Shape Phenotypic Plasticity. **Bioessays**. 40 (2). 2018.
2. 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** - (Accepted)
3. 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. **BioRxiv** 445023.
4. Sanchez-Valle J, Tejero H, Fernandez JM, Juan D, Capella S, Al-Shahrour F, Tabares-Seisdedos R, Pancaldi V, Valencia A. Unveiling the molecular basis of disease co-occurrence: towards personalized comorbidity profiles. **BioRxiv** 431312.

Technology Cluster

Manager: Frédéric Lopez

The CRCT's Technology Cluster contains several technical resource centers whose expertise and facilities are available to the entire campus. Ten engineers provide open-access training in using the Cluster's facilities and help researchers design projects and experiments, interpret and present research findings, write publications and valorize results.

In 2018, the Technology Cluster obtained dual ISO 9001:2015/NFX 50-900 certification for all its expertise, R&D and training services. These certifications are valid for three years and will be subject to annual auditing and monitoring.

The cluster contains 8 technical resource centers:

- Proteomics (biochemistry, mass spectrometry) and molecular interactions (Biacore technology)
- Flow cytometry and cell sorting
- Imaging (confocal microscopy and video microscopy)
- Vectorology (L3 laboratory)
- Genomics and transcriptomics
- Monoclonal antibody production
- Bioinformatics
- Biological resource center (malignant blood disorders biobank)

Thanks to funding from the latest "Contrat Plan Etat Région" and support from CRCT team 13, led by Prof. H. Avet-Loiseau, in 2018 the Technology Cluster was able to procure:

- A high-speed FACS Aria Fusion Cytometer (BD)
- A FACSMelody cell sorter (BD)
- A Chromium Single Cell Gene Expression (10X Genomics): creation of cDNA libraries from single cells
- A NextSeq 550 sequencer (Illumina)
- An Operetta CLS High-Content Analysis System (Perkin Elmer)

In addition, an Xrad Smart Irradiator, co-financed by the ICR and Inserm Plan Cancer, has just been installed.

www.poletechno-crct.inserm.fr/



CRCT – IUCT-O interconnections

In 2018, the CRCT received an evaluation visit from its International Scientific Council in preparation for the five-yearly appraisal by the High Commission for Evaluating Research and Higher Education, scheduled for November 2019. The results were very positive, as this extract from the International Scientific Council's report shows:

"The Cancer Research Center of Toulouse (CRCT) is an excellent and internationally leading research centre that fosters novel breakthroughs for the cancer problems, from understanding the molecular details of cancer to addressing with novel treatments in the clinic. The centre is committed to a team science approach where basic, applied scientists and clinicians work together to achieve translational goals. Numerous novel projects are developed, progressed and have generated impact on a global scale, often in collaboration with research teams across France and also internationally. The new building and closeness to the

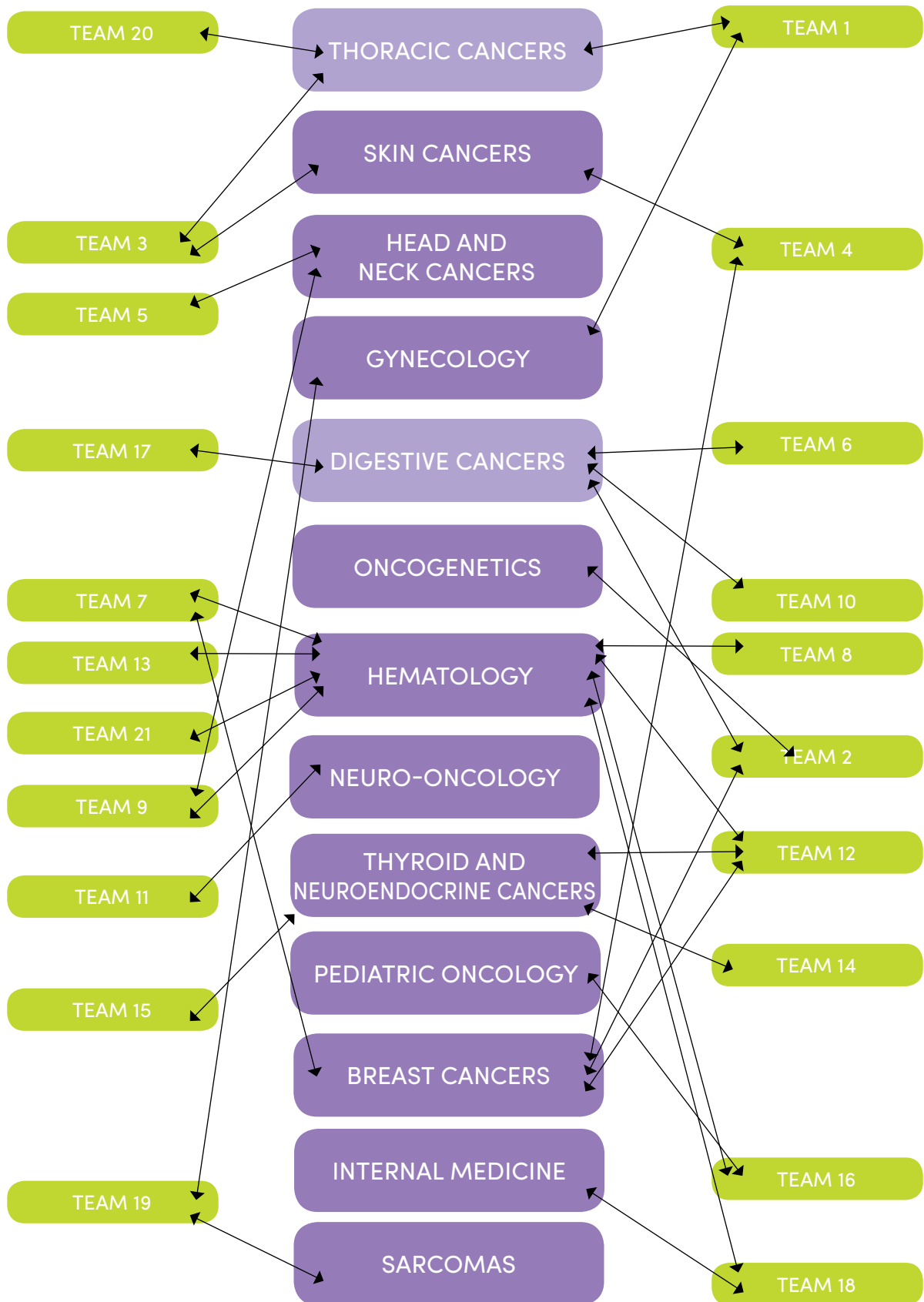
clinic is excellent and the interactions with clinicians are frequent and real. A few areas are outstanding and in particular myeloma, which has developed amazingly over the last few years. Sarcoma, lymphoma, pancreas, glioblastoma and lung cancer are areas under suitable development that have good potential to flourish under the next 5 years. There are many pre-clinical projects of excellent quality which are internationally competitive and more major grants, such as from the ERC, are expected to come within the next 5 years. The CRCT is a well working organisation and the spirit and results are overall excellent!"

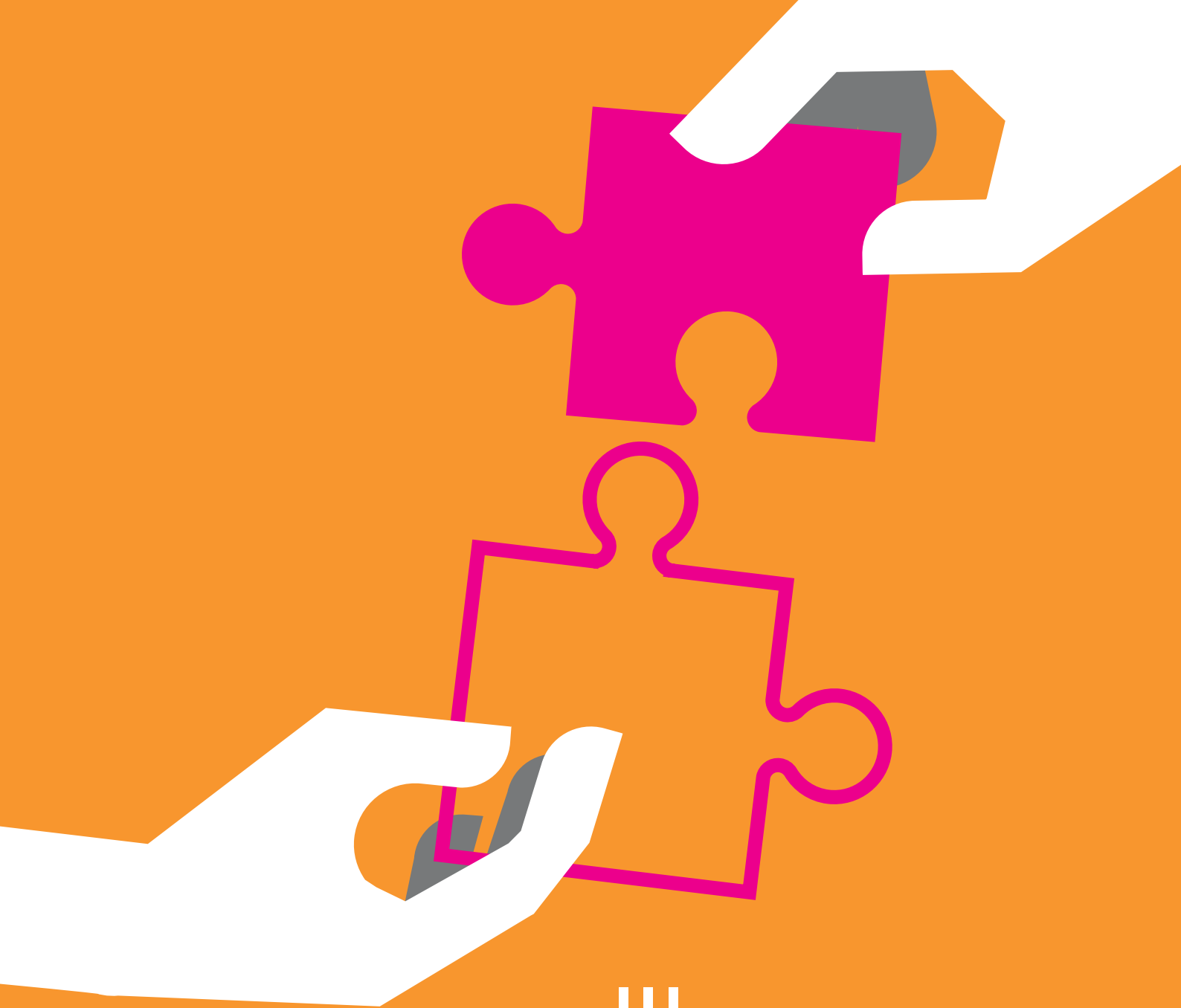
The excellent results obtained in 2018 are largely due to the close links created between research and treatment. The diagram on the following page charts these interconnections between the IUCT-Oncopole's research teams and clinical teams.

Members of the CRCT's International Scientific Council:

Prof. Thomas Helleday (President), University of Sheffield, United Kingdom, & Stockholm University/Karolinska Institutet, Sweden – Dr. Bruno Goud (Vice-President), Institut Curie, Paris, France – Dr. Reuven Agami, Netherlands Cancer Institute, Amsterdam, Netherlands – Dr. Jean-Marc Egly, IGBMC, Illkirch, France – Prof. Michel Cogné, CRIBL, Université de Limoges, France – Prof. Brunangelo Falini, Università degli studi di Perugia, Italy – Dr. Stéphane Germain, CIRB Collège de France, Paris, France – Prof. Catherine Ghezzi, LRB, Université de Grenoble Alpes, France – Prof. John Hickman, University of Manchester, United Kingdom, & Servier/IMI Preduct, Paris, France – Prof. Gillies McKenna, CRUK/MRC, University of Oxford, United Kingdom – Dr. Jacques Pouyssegur, IRCAN, Nice, France & Centre Scientifique de Monaco – Prof. Roland Schmid, Technische Universität München, Germany – Prof. Daniel Speiser, Université de Lausanne, Switzerland – Dr. Michele Trabucchi, C3M, Nice, France – Dr. François Vallette, CRCINA, Nantes, France – Prof. William Vainchenker, Institut Gustave Roussy, Villejuif, France – Prof. Benoît Van den Eynde, Université Catholique de Louvain, Belgium, & Ludwig Institute for Cancer Research, Brussels, Belgium/University of Oxford & Ludwig Institute for Cancer Research, Oxford, United Kingdom.

Research-treatment interconnections





HEALTHCARE AND CLINICAL
RESEARCH

Key figures

34,397 patients treated in 2018 (+3.3% compared with 2017), including **10,112** new patients who came to the technical centers or the consultation, radiotherapy or hospitalization departments (+2.3% compared with 2017).

2,673 patients received oral therapies (+8.6% compared with 2017)

105,289 hospital stays (+1.7% compared with 2017), including **58,134** radiotherapy sessions (+1.03% compared with 2017)

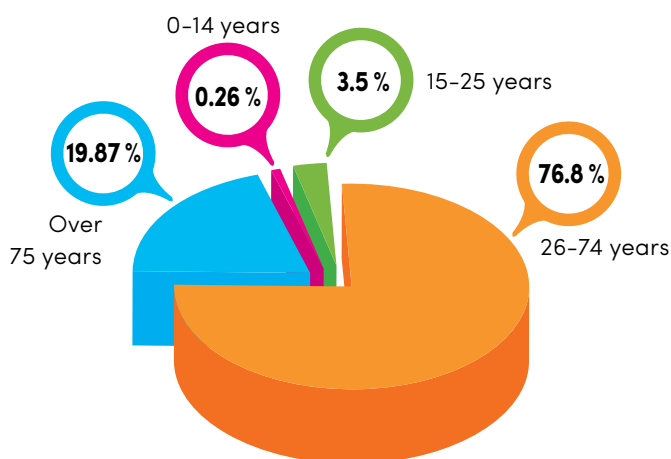
190 transplants : **65** allogenic transplants and **125** autologous transplants (hematology and solid tumors)

79% outpatients in the hospitalization departments

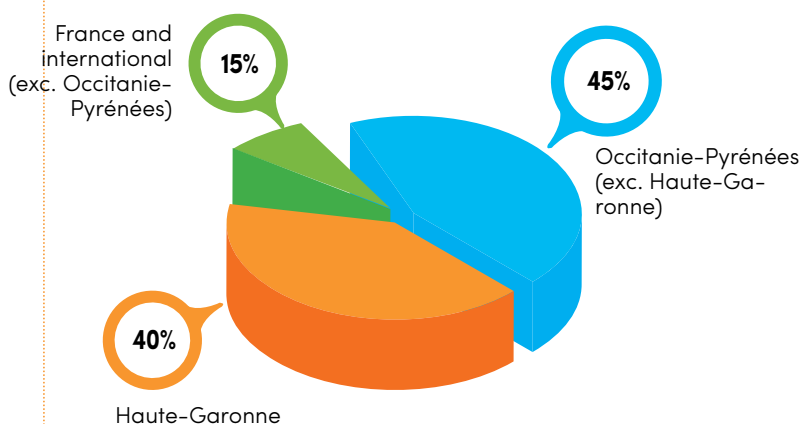
44.04% men
55.96% women

183 clinical trials included
1,520 IUCT-Oncopole patients, that is, 15.03% of patients (active files)
51.9% of trials were early phase

Distribution by age group



Geographical origin of patients



Patient care pathways

Patient care at the IUCT-Oncopole is based on a multidisciplinary approach that ensures every patient receives the best possible treatment. Patient files are reviewed at weekly multidisciplinary team (MDT) meetings, which draw up an appropriate, personalized and innovative treatment program for each patient. What is more, the IUCT-Oncopole's unique structure, which combines the specialties needed to detect, treat and monitor all types of cancer with state-of-the-art technical facilities, enables it to offer patients optimal therapy programs that incorporate the latest advances in diagnosis and treatment.

Direct access to innovation

Thanks to the close links between the hospital's clinicians, supported by the Research and Innovation Department, the CRCT's research teams, and the CLIP² (early phase trials – INCa) accreditation awarded to the Clinical Trials Office, it takes less than six months for a laboratory discovery to be transferred to a clinical trial at the IUCT-Oncopole. This approach is part of France's 2014-2019 Cancer Plan, whose objectives include increasing the number of patients included in cancer clinical trials (the target is 50,000 inclusions in 2019 for all trials conducted in France).

The IUCT-Oncopole's clinicians and paramedical staff also sponsor a wide range of research projects aimed at evaluating existing healthcare practices and testing innovative procedures.

What is more, teams take all necessary measures to ensure innovative techniques are deployed under the best possible conditions. For example, several departments and units worked together throughout 2018 in order to prepare for the arrival of CAR-T therapy (Chimeric Antigen Receptor T-cell) in 2019.

Next generation digital tools

For patient reception

Self-check-in terminals and information screens were fitted in the Reception and Consultations Department in 2018 in order to improve patient flow and comfort. These new facilities reduce the number of times patients have to come to the Admissions Office, simplify the admissions process and provide patients with important information such as their consultant's name, appointment time, waiting room number, estimated waiting time and directions.

For coordinating patient care

In 2018, the IT department began the process of setting up a Computerized Patient File system and a "city-hospital" liaison platform. By holding a series of consultations with the healthcare teams in order to define needs and choose the best IT solutions. The new system, due to come into service in 2019, will provide clear, real-time information on each patient's treatment protocol and help coordinate the arrangement of appointments with different healthcare professionals.



It will also allow the IUCT-Oncopole to communicate more effectively with outside bodies by ensuring that information is shared between all three IUCTs, by incorporating the Shared Medical Record system (*Dossier Communicant de Cancérologie*) and by strengthening links with other healthcare partners.

For home monitoring

As more and more patients receive their treatment as outpatients and/or as oral therapies, it has become necessary to develop new ways of monitoring patients at home. Consequently, 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). A second-generation system, developed in association with MHComm, is based round a secure cell-phone app called "Mon E-suivi IUCT Oncopole". A survey found that 96.7% of the 35 outpatients who took part in an INCa-supported pilot study (PICTA, coordinated by Dr. A. Daboussi) in 2018 were satisfied with the system, 93% said it made them feel safer and 97% found it easy to use. Officially launched in January 2019, the system comprises seven programs for surgery, oncology and hematology outpatient pathways and for nutritional monitoring of radiotherapy patients.

Care for specific sectors of the population

Treating younger and older patients requires specific approaches adapted to their particular medical, biological and psychosocial characteristics.

A regional referral center for adolescents and young adults (AYA)

The IUCT-Oncopole is a NetSarc national referral center (INCa accredited) for bone sarcomas. In addition, in 2017, a specially designed activities room equipped with a graffiti mural, a big screen TV, video games, a "pro" table football game and an XXL couch was set up in order to provide AYA patients with a fun and easy-going environment in which to relax. As a further measure for AYA patients, a regional coordination unit (AJAMIP) was set up in 2018 at the initiative of the General Directorate for Healthcare Services (DGOS) and with support from the Regional Health Agency. It will bring together a variety of tools to help hospital clinicians, family practitioners, patients and patients' families understand the specificities of caring for AYA patients. A list of patient associations has already been drawn up and posted on the website of Onco-Occitanie regional cancer network. AJAMIP's main objectives include helping healthcare units that see very few AYA patients improve the care they provide to young patients.

Older patients: expert care and access to innovation

Treatment pathways for older cancer patients are determined in the light of each patient's overall health (possibility of multiple pathologies) and his or her independence and family situation. The Oncogeriatrics OCC (coordinators: Dr. L. Mourey & Dr. L. Balardy), in conjunction with the IUCT-Purpan, consider all these parameters when drawing up treatment programs, in order to find the best compromise between efficacy and quality of life.

Older patients were long excluded from clinical trials because of the heterogeneity of this population. However, an IUCT-Oncopole team, coordinated by Dr. L. Mourey and T. Filleron and working in collaboration with the Institut Curie (Paris) and the Institut Paoli-Calmettes (Marseille), has now drawn up methodologies that enable clinical trials to take into account this heterogeneity. This research was carried out as part of a project funded by the Ligue Contre le Cancer. The team also designed a software package (R

package) that is available from the CRAN website as freeware and therefore open to all members of the scientific community.

Integrated supportive care

The IUCT-Oncopole is unusual among cancer centers in that it has a dedicated supportive care department (DISSPO), whose multidisciplinary activities are transversal and at the interface between the healthcare departments and the Organ Coordination Committees (OCC).

Introduction of dental hygiene consultations

In 2018, the consultations department began providing paramedical dental hygiene consultations to all radiotherapy patients and to other inpatients referred to the department by healthcare teams. Two dental assistants – S. Betancourt and C. Teulières – ensure each patient receives a consultation prior to treatment and during the post-treatment monitoring phase. This consultation is in addition to the dentistry treatments provided by Dr. E. Vigarios (diseases of the oral mucosa)

A “city-hospital” liaison system under test

The General Medicine and Medical Oncology Departments, the Onco-Occitanie regional cancer network and ARS Occitanie have designed a strategy to strengthen coordination between family practitioners and the hospital and thereby improve treatment pathways for patients with metastatic solid tumors. The new strategy is centered round family practitioners who have received extra training in cancerology (DESC) and who work part time in cancer care centers in order to coordinate structured “return home” consultations in conjunction with the patient’s family doctor. For the test phase, five DESC family practitioners have been placed in cancer centers across the Toulouse healthcare catchment area, including the IUCT-Oncopole. These family practitioners dedicate half their time to the system (the other half is spent in general practice). By facilitating information sharing between caregivers and enabling them to better anticipate each patient’s needs, the system should reduce unplanned visits to specialist healthcare centers and thereby enable patients to remain in their own “healthcare areas” without compromising the quality of care. Trials of the new system, known as CREDO, were launched in September 2017 and will continue for 3 years (825 patients will be included) under the supervision of Prof. M-E. Rougé-Bugat. The work has been funded by a DGOS (PREPS) grant.

and Dr. M. Boulanger (oral surgery).

A “Sport and Cancer” dynamic...

A fitness/wellness garden was opened on the lawns at the IUCT-Oncopole in 2016. Harmoniously planted with 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 place in which to relax. Hedges form secluded corners in which patients can do the exercises prescribed by their physiotherapist and the Physical Medicine and Rehabilitation team.

...that continues outside the IUCT-Oncopole’s walls

The IUCT-Oncopole’s Sport & Cancer Center is one of eight such centers funded by CAMI Sport et Cancer and its partners across France. Opened in 2017, it offers cancer patients free access to specially designed group physical activity sessions. In 2018, Stade Toulousain Rugby Club joined the program by providing sports therapy sessions at the Ernest-Wallon Stadium of Toulouse.

Also on a rugby theme, in 2017, Dr. S. Motton introduced 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 invites women cancer patients to join caregivers for a weekly game of 5-a-side rugby. These sessions fall within the French Rugby Federation’s “sport and health” protocol and are greatly appreciated by patients. In 2018, the Midi-Pyrenees Sports Medicine Society awarded Rubies its Michel Lagarrigue Prize.

Partner charities

Several charities work closely with the IUCT-Oncopole, often through volunteers who offer patients moments of companionship and support. Special programs run by some of these charities include Cheer Up, which helps young patients look beyond their cancer and draw up projects for the future, CAMI, which organizes adapted sports and physical activity sessions on prescription, and La Vie Entre les Mains, which provides beauty care to both inpatients and outpatients. In addition, patients and their families can access a wide variety of services, information and advice from the Ligue Contre le Cancer’s Haute-Garonne branch, which has an office in the Oncopole’s Community Center.

Clinical research

Member of numerous INCa clinical research networks

The IUCT-Oncopole was one of the first three members of the **CLIP² network of INCa-accredited early phase trials centers** (coordinator: Prof. J.-P. Delord). In addition, the IUCT-Oncopole (through the ICR), Bordeaux University Hospital, the Institut Bergonié and Montpellier Regional Cancer Institute have set up a "Greater Southwest Network of Early Phase Trials Centers".

It is also a member of the INCa-approved National Investigation Group for Studies of Ovarian and Breast Cancers (**GINECO**). Dr. L. Gladiéff is both the GINECO coordinator for the IUCT-Oncopole and the group's president.

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.

A quality-accredited structure

- In 2013, the Institut Claudius Regaud became one of France's first cancer clinical research establishments to obtain ISO 9001 certification, alongside the Institut Paoli Calmettes (certified by Veritas). In 2017, 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. The certification obtained in 2015 covers "project management within the research and innovation department of Toulouse University Hospital: promotion and partnerships". Internal promotion, partnerships, valorization, project implementation processes and the support processes involved in managing research projects were all audited by AFNOR (France's standards organization).



Methodology Research to optimize clinical trials

As well as providing methodological support to the Clinical Trials Office, the Biostatistics Unit, coordinated by T. Filleron, carries out research into ways of improving the statistical processing of therapeutic trials. In 2018, the unit worked with Toulouse School of Economics on two projects aimed at optimizing the duration and frequency of post-therapeutic monitoring and at optimizing methods for selecting variables for high dimension data. In addition, as part of 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 Oncogeriatrics Department.

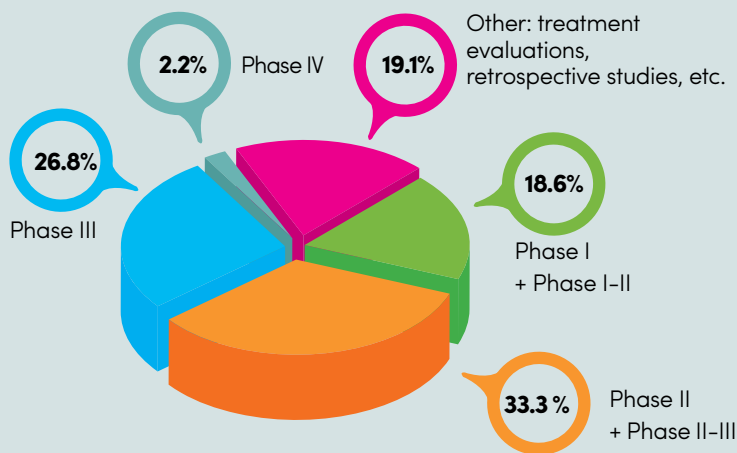
Innovative collaborations

Discussions with industrial companies aimed at strengthening or finalizing collaborations led to the signing of several framework agreements with international clinical research networks during 2018, most notably in the field of immuno-oncology: imCore (Genentech), GECL (Bristol-Meyers Squibb), OTX (Novartis), etc. The IUCT-Oncopole was the first center in France to sign a Master Agreement with the imCore network.

Clinical research indicators

183 clinical trials, including 53 IUCT-Oncopole-sponsored multi-center trials, recruited patients in 2018
1,941 patients, including 1,520 patients from the IUCT-Oncopole (**15.03%** of active file), were included in a clinical trial in 2018
51.9% of trials were early phase
28.9% of clinical trials were sponsored by the IUCT-Oncopole

Percentage of patients included by trial phase



28.4% of patients included in trials sponsored by other academic institutions



Research projects

Numerous projects obtained funding in 2018, including four projects that received grants (2 PHRC-K and 2 PRTK grants) from France's General Directorate for Healthcare Provision.

BLAD-RAD001

Led by Dr. J. Khalifa. Awarded a PHRC-K grant in 2018

BLAD-RAD001 is a phase II prospective study to evaluate consolidative radiotherapy in patients with metastatic urothelial cancer of the bladder in partial or complete response and with at least three residual metastatic lesions after first-line systemic therapy. Ancillary studies will be conducted to investigate a radiomics signature that can be used to predict the benefits of consolidative treatment, radiobiological markers of radioresistance and modifications to tumor cells and the microenvironment between pre-chemotherapy and post-chemotherapy.

CINSARC signature

CINSARC is a molecular signature of 67 genes that was identified in 2010 by Dr. F. Chibon and optimized for routine use by T. Lesluyes and Dr. S. Le Guellec:

- **CHIC-ST01 trial, sponsored by Dr. T. Valentin – 2018 PHRC-K grant**

The purpose of this trial is to assess the value of perioperative chemotherapy in patients with localized, grade-1 or grade-2 soft-tissue sarcomas and identified as being at high risk by their CINSARC signature.

- **MIRAS-SARRA, sponsored by Dr. F. Chibon and Dr. T. Valentin – 2018 PRTK grant**

The study's aim is to determine the immune landscape profiles of nine rare (<1%) subtypes of soft tissue sarcoma (STS) for which treatments extrapolated from "frequent" forms of STS are inappropriate. This will be done by simultaneously analyzing CINSARC transcrip-

tomeric signatures, tumor infiltration of immune populations and the expression of Cancer Testis Antigens, in order to determine how these factors impact tumor behavior and clinical outcomes. The study will analyze more than 500 tumors from the French Sarcoma Group (GSF) database.

LUNG-RESIST

Sponsored by Prof. J. Mazières, Prof. G. Faver and Dr. I. Rouquette – 2018 PRTK grant

LUNG-RESIST's aim is to understand and prevent adaptive resistance to third-generation targeted anti-EGFR lung cancer therapies. This will be done by using state-of-the-art technologies such as patient-derived xenografts (PDX) and circulating tumor cells (CTC) to comprehensively characterize phenotype and molecular modifications. The results should suggest new therapeutic approaches for eliminating the reservoir of drug-resistant cells and preventing the appearance of resistance mutations that lead to patient relapse.

The IUCT-Oncopole is also a partner in a Horizon 2020 research 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). Its purpose is to explore the effects of exposure to low doses of radioactivity. MEDIRAD consists of six interdependent Work Packages, one of which (WP3 – coordinator: Dr. G. Flux) will examine the doses of iodine 131 needed to treat thyroid cancers. CRCT team 15 (leader: Dr. M. Bardiès) is providing expertise in dosimetry for this project (dosimetry axis) and the IUCT-Oncopole is the only French institution involved in the clinical study (coordinator: Prof. F. Courbon).

This H2020 project's overall goal is to improve the sci-

entific bases and clinical practice of radiation protection in the medical field and thereby 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.).

In addition to clinical trials conducted in collaboration with the CRCT, the IUCT-OncoPole's OCCs and clinical departments also carry out many research projects of their own. Here are a few examples:

Liquid Biopsies

The Oncology Medical Biology Laboratory's (LBMO) Exploratory Biology Unit (managers: Prof. G. Favre & Dr. A. Pradines) is highly involved in clinical research, innovation and the medical-economic evaluation of cancer liquid biopsies. It also plays an active role in translational research, running a technical center (Nanostring technology), and in helping the CRCT design novel projects. In addition, it carries out its own projects, in collaboration with CRCT team 3, with the aim of developing new circulating biological markers for diagnosis, prognosis, longitudinal monitoring of cancers and predicting therapeutic responses. These markers include circulating nucleic acids (RNA, then DNA), circulating tumor cells and, more recently, circulating immune cells. Thanks to its extensive expertise, the Exploratory Biology Unit is able to provide a wide range of circulating biomarker analyses for clinical trials.

Pharmacokinetics & Pharmacogenetics

The PHACS project ("Pharmacokinetics of tamoxifen and anti-aromatases, correlation with pharmacogenetic characteristics"), which was coordinated by the LBMO's Pharmacology (manager: Prof. E. Châtelut) and Pharmacogenetics (manager: Dr. C. Toulas) Units, examined correlations between the pharmacokinetic and pharmacogenetic parameters of hormonal treatment adjuvants (tamoxifen) for breast cancer. Inclusions ended in 2018 (more than 2,000 patients) and the first results were published at the beginning of 2019.

The Pharmacogenetics Unit also carries out pharmacodynamics projects (metabolism and aromatases), while the Pharmacology Unit carries out research into other types of drugs (tyrosine kinase inhibitors and immune checkpoint inhibitors) and radioactive tracers. It was also one of the first academic teams to study population pharmacokinetics and is now looking at using this approach to study radioactive tracers.

Clinical immunological monitoring

The LBMO's Immunity Monitoring Unit (manager: Prof. M. Ayyoub) was set up in 2017 to meet the needs of IUCT-OncoPole clinicians involved in developing immunotherapies. Its primary objective is to identify the biological bases of immunotherapy responses and toxicity. As well as monitoring patients undergoing treatment, the unit runs specially adapted monitoring protocols for immunotherapy clinical trials. It also uses the results of research carried out at the CRCT (team 1) to develop new trials, such as the MINER study into immunological mechanisms and biomarkers that can be used to monitor the efficacy and toxicity of immunotherapy treatments for different cancers (melanomas, lung, bladder, head and neck, etc.). Sponsored by Prof. J.-P. Delord, MINER was launched in 2018 after receiving funding from the imCore network and the MSD Avenir foundation. Other new trials are planned for 2019.

Artificial Intelligence

An artificial intelligence project was launched at the end of 2018. Developed in partnership with MH-Comm, Alcimed and the CEA and sponsored by Prof. J.-P. Delord, its goal is to develop a demonstrator capable of realistically simulating the supervision of breast cancer patients receiving treatment at home. In addition, the first Artificial Intelligence Call for Expressions of Interest awarded a grant to another AI project in 2018. This project, which is sponsored by Dr. C. Franchet, will begin in 2019 by developing an AI tool capable of examining pathology reports and extracting and structuring the medical information needed to take post-operational decisions during MDTs. Other ongoing projects include COMPUTREAT 2015-2019, steered by Prof. L. Ysebaert (Hematology OCC) in collaboration with Toulouse Mathematics Institute

(IMT) and the IUCT-Oncopole's medical physics team, whose purpose is to develop a model to predict relapses in patients undergoing treatment for chronic lymphoid leukemia.

Clinical trials methodology

The Methodology-Biostatistics Unit, coordinated by T. Filleron, carries out research to improve the statistical processing of therapeutic trials. In 2018, the unit worked with Toulouse School of Economics on two projects aimed at optimizing the duration and frequency of post-therapeutic monitoring and at optimizing methods for selecting variables for high dimension data. In addition, as part of 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.

Collaborations with other research laboratories in Toulouse

Many IUCT-Oncopole clinicians are also members of other research laboratories in Toulouse which are exploring other avenues for combatting cancer:

- Prof. L. Laprie (Radiotherapy Department) is a member of the DEVIN team (manager: Dr. P. Peran) at Toulouse Neuro-Imaging Center (ToNIC), an Inserm and University of Toulouse III-Paul Sabatier mixed research unit. DEVIN's research focuses on the brain and its main pathologies, especially brain tumors, ballistics and cognition.
- Dr. C. Vaysse (Surgery Department) is a member of the Microenvironment, Cancer and Adipocytes team (manager: Prof. C. Muller) at the Institute of Pharmacology and Structural Biology (UMR5089 CNRS – IBPS), which mostly studies links between obesity and breast cancer.
- Dr. A. Dupret-Bories (Surgery Department) is part of the CIRIMAT (UMR CNRS INPT UPS 5085 / director: Prof. C. Laurent). In 2018, CIRIMAT launched a project to develop a biomaterial capable of stimulating bone regeneration in cases of osteoradionecrosis. It also began a collaborative project with Rescoll to develop a gel to reduce pharyngeal fis-

tulas following a total laryngectomy. Another collaboration with the Toulouse company AnatomikModeling resulted in a method for using 3D printing to produce custom-cutting guides and mandible and maxilla phantoms. This method will greatly benefit patients with head and neck cancers, as it reduces surgery times, improves survival rates for bone grafts, and ensures better functional results. Dr. Dupret-Bories also coordinates the in-vivo axis of the Ti-Polti project (funded by Institut Carnot MICA), whose aim is to develop new osteosynthesis plates that reduce the risk of rejection.

- Dr. P. Grosclaude is on secondment to the 5-EQUITY team at the UMR 1027 mixed research unit (manager: Dr. C Delpierre). His work centers round epidemiological studies of cancers.
- In 2018, Dr. S. Ken (Engineering and Medical Physics Department) joined the Informatics Research Institute of Toulouse's (IRIT) MINDS team (manager: Dr. A. Basarab) as an associate researcher, in order to develop advanced analytical and image interpretation tools.

Organ Coordination Committees

In order to ensure each patient receives the most appropriate integrated care according to his/her pathology, the IUCT-Oncopole's healthcare professionals are organized into Organ Coordination Committees (OCCs). The OCCs:

- Organize care pathways and help ensure patients receive the best quality care;
- Define the frequency and format of MDT meetings, in conjunction with France's Cancer Coordination Center network;
- 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;
- Determine needs in terms of personnel and facilities;
- Organize clinical and translational research in the OCC's field
- Help train experts and future professionals

Twelve OCCs are fully integrated within the IUCT-Oncopole and a further three OCCs are shared with the IUCT's other sites. All 15 OCCs are listed below, together with their coordinators.

IUCT-O OCC	
BREAST CANCER	Prof. Florence Dalenc – Dr. Eva Jouve – Dr. Charlotte Vaysse
GYNECOLOGY	Dr. Laurence Gladieff
SARCOMAS	Dr. Christine Chevreau
HEMATOLOGY	Prof. Christian Récher
SUPPORTIVE CARE	Dr. Nathalie Caunes-Hilary – Prof. Virginie Woisard
HEAD AND NECK CANCERS	Prof. Sébastien Vergez – Dr. Michel Rives
NEURO-ONCOLOGY	Prof. Elizabeth Moyal – Dr. Delphine Larrieu-Cirron
ONCOGENETICS	Prof. Rosine Guimbaud – Dr. Viviane Feillel
SKIN CANCERS	Prof. Nicolas Meyer – Dr. Dimitri Gangloff
ONCOGERIATRICS	Dr. Loïc Mourey – Dr. Laurent Balardy
THYROID AND NEUROENDOCRINE CANCERS	Prof. Frédéric Courbon – Prof. Rosine Guimbaud – Prof. Delphine Vezzosi
UROLOGIC CANCERS	Prof. Bernard Malavaud – Dr. Loïc Mourey – Dr. Pierre Graff-Cailleaud
Associated OCCs	
DIGESTIVE CANCERS	Prof. Rosine Guimbaud
THORACIC CANCERS	Prof. Julien Mazières
PEDIATRIC ONCOLOGY	Prof. Anne Laprie – Dr. Marie-Pierre Castex

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 IUCT-Oncopole OCC, it is described as such in the following pages.

IUCT-O OCC: BREAST CANCER

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

Activity	Active files (change compared with 2017)
Total	2,627 (-0.38%)
Surgery	1,483 (-1.92%)
Chemotherapy	1,175 (+1.47%)
Radiotherapy	976 (+7.02%)

42 physicians
35,413 hospital stays (+4.6% compared with 2017)
2,627 patients (-0.38% compared with 2017)
18,670 consultations (+1.2% compared with 2017)
29 trials open, including one phase I-II trial

Strategic objectives: The Breast Cancer OCC focuses on four major objectives:

Optimize care pathways: structure the monitoring stage and introduce a personalized decision-making mechanism for MDT meetings; Expand clinical research: sponsor more clinical trials and carry out trials relating to every aspect of the Breast Cancer OCC's work; Integrate metabolism-centered translational research into clinical activities: sterols – breast cancer – adipocytes axis; Optimize regional cooperation with respect to training and research.

• **A regional referral center for breast cancer radiology**

The IUCT-Oncopole's Imaging Department's dedicated breast cancer radiology unit plays a crucial role in preventing, detecting and choosing treatments for breast tumors in women at risk. In 2018, the unit acquired a tomosynthesis machine (3D mammography), whose high-resolution images make it easier to differentiate between tumors and healthy tissue.

• **Two regional collaborations for knowledge sharing**

Following the formation of the Occitanie Region, the IUCT-Oncopole began discussing possible knowledge-sharing initiatives with cancer care institutions in Montpellier. These discussions have resulted in the creation of an "interuniversity diploma" in "Breast Cancer: from physiology to after cancer", which will receive its first students in February 2019, and the organization of the first Occitane Breast Cancer Meeting, which will be held in 2019 under the auspices of the Onco-Occitanie network.

• **A mobile app under test**

Funding from the Ligue Contre le Cancer and GIRCI-SOHO has enabled the OCC to launch a pilot study to evaluate a systematic e-monitoring system for breast cancer patients undergoing adjuvant hormonal therapy. In addition to providing advice and support, the app-based system should facilitate the early detection and treatment of side effects and have a positive impact on adherence to treatment.

• **MARTA project awarded a PHRCI 2018 grant**

MARTA (coordinator: Dr. C. Massabeau) is a multi-

center prospective study to evaluate surgical breast cancer treatment by mastectomy with immediate prosthetic reconstruction in patients requiring an adjuvant treatment (radiotherapy carried out as tomotherapy +/- chemotherapy). The project, which is being run in collaboration with the radiology department, was awarded a PHRCI 2008 grant.

• **EPOXCAN – continuing research into DDA**

Research conducted in 2017 in collaboration with CRCT team 12 (Dr. M. Poirot and Dr. S. Silvente-Poirot) established a link between a cholesterol derivative, dendrogenin A (DDA), and cancerous tumors. A project to further investigate the role the metabolic deregulation of DDA plays in breast cancer has been funded via a Translational Research@IUCT-Oncopole grant. The IUCT-Oncopole's pharmacokinetics team (Prof. E. Chatelut) will carry out the metabolic dosing section of the project.

Main collaborations: CRCT teams 2 (Dr. J-S. Hoffmann), 4 (Prof. T. Levade & Dr. N. Andrieu), 7 (Prof. P. Brousset), 12 (Dr. M. Poirot & Dr. S. Silvente-Poirot), and with the "Cancer Microenvironment and Adipocytes" team at UMR5089 CNRS-IPBS (Prof. C. Muller).

Selected publications in 2018:

- . Cottu, P. et al. Letrozole and palbociclib versus chemotherapy as neoadjuvant therapy of high-risk luminal breast cancer. *Ann. Oncol.* (2018).
- . Gui, P. et al. The Protease-Dependent Mesenchymal Migration Of Tumor-Associated Macrophages As A Target In Cancer Immunotherapy. *Cancer Immunol Res* (2018).
- . Silvente-Poirot, S., Dalenc, F. & Poirat, M. The Effects of Cholesterol-Derived Oncometabolites on Nuclear Receptor Function in Cancer. *Cancer Res.* (2018).

IUCT-O OCC: GYNECOLOGY

Coordinator: Dr. Laurence GLADIEFF

Activity	Active files (change compared with 2017)
Total	794 (+5.59%)
Surgery	401 (+5.8%)
Chemotherapy	359 (+14.7%)
Radiotherapy	145 (+9.85%)
Brachytherapy	157 (+12.85%)

17 physicians

5,722 hospital stays (+6.42% compared with 2017)

794 patients (+5.59% compared with 2017)

3,541 consultations (+2.8% compared with 2017)

12 trials open, including 2 phase I-II trials

The IUCT-Oncopole, via the ICR, is a European Society of Gynecological Oncology (ESGO) accredited training center for gynecological oncology.

Strategic objectives: The Gynecology 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.

• INCa-accredited regional referral center

The IUCT-Oncopole, via the ICR, 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).

• Strong involvement in national cooperation groups

Through its members, the OCC is also affiliated with several cooperation groups and learned societies, notably the French Society for Gynecological Oncology (SFOG), the INCa-accredited National Group of Ovarian and Breast Cancer Investigators (GINECO), whose vice-president in 2017 was Dr. L. Gladieff, and the Francophone Society for Oncological Surgery (SFCO), whose vice-president is Dr. G. Ferron.

• Contribution to drafting national guidelines

In 2018, several of the OCC's physicians helped draft both the INCa's Guidelines for Clinical Practice for the first-line treatment of ovarian cancers and updates to the Saint Paul de Vence guidelines for clinical practice, which will be presented at the 18th Francophone Conference on Breast and Gynecological Cancers in 2019.

• A ten-step guide to gynecological surgery

In 2018, Drs. C. Martinez-Gomez, M.A. Angeles, A. Martinez and G. Ferron wrote a series of ten-step guides to different surgical techniques. Each guide

was accompanied by a specially made video illustrating its content. These clear and easy-to-follow tools attracted the attention of the Spanish Academy of Medicine and Surgery, which awarded them its Jose Abril Morales Prize. The series will be continued in 2019.

• Using sport to improve patients' overall well-being

The OCC's Dr. S. Motton is the founder and president of Rubies, France's first "rugby for health" club. Created in 2017, this novel initiative enables patients and caregivers to come together for weekly 5-a-side rugby training sessions. As well as being part of a "sport for health" protocol sponsored by the French Rugby Federation, it is greatly appreciated by patients and was awarded the 2018 Michel Lagarrigue Prize by the Midi-Pyrenees Sports Medicine Society.

Main collaborations: CRCT teams 1 (Prof. M. Ayyoub) and 19 (Dr. F. Chibon).

Selected publications in 2018:

. Angeles, M. A., Martínez-Gómez, C., Martínez, A. & Ferron, G. En bloc pelvic resection for ovarian carcinomatosis: Hudson procedure in 10 steps. *Gynecol. Oncol.* (2018).

. Martínez, A. et al. Prospective Assessment of First-Year Quality of Life After Pelvic Exenteration for Gynecologic Malignancy: A French Multicentric Study. *Ann. Surg. Oncol.* 25, 535–541 (2018).

. Martínez-Gómez, C., Angeles, M. A., Martínez, A. & Ferron, G. Laparoscopic anterior pelvic exenteration in 10 steps. *Gynecol. Oncol.* (2018).

IUCT-O OCC: SARCOMA

Coordinator: Dr. Christine CHEVREAU

Indicator	Number (% change compared with 2017)
MDT meetings	49 (-2%)
MDT records	1,182 (+7.26%)
Patients	670 (+6.25%)

14 physicians
307 new patients per year
16 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. Bonneville and Dr. C. Chevreau.

Strategic objectives: The Sarcoma OCC is continuing to structure regional care provision for patients 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.

• A national expertise center

The IUCT-Oncopole, via the ICR, is one of 17 INCa-designated centers of excellence within the NetSarc (soft-tissue sarcomas) and RESOS (bone sarcomas) referral networks. Through its members, the Sarcoma OCC is also a center of expertise within the RRePS pathology network, for which it provides second opinions on every new case of sarcoma.

• Founder member of the SARRA group

SARRA, a subgroup of the French Sarcoma Group (GSF), focuses on nine rare (<1%) types of Soft Tissue Sarcoma (STS) for which treatments extrapolated from "frequent" forms of STS are inappropriate. The IUCT-Oncopole was chosen to manage and analyze the group's databases.

• Initiating a structured approach to treating AYA patients

The structure underlying the provision of care to AYA cancer patients (15 – 25 years old) at the IUCT-Oncopole is based on a model developed by the Sarcoma OCC. This model, which is now well established and approved by the INCa, brings together the AYA-adult solid tumors group (Dr. C. Chevreau), AYA-adult hematology group (Dr. F. Huguet), AYA-pediatric solid tumors group (Dr. M-P. Castex) and AYA-pediatric hematology group (Dr. G. Plat). The OCC, in conjunction with the Onco-Occitanie network, also helped create a group, known as AJAMIP, to oversee the provision of care to AYA patients.

• 2018 PRTK and PHRC-K grants for research

The MIRAS study, a SARRA group project that was drawn up in collaboration with the ONCOSARC team,

has been awarded PRTK funding. Its aims are to draw profiles of the immune landscapes of the rare sarcomas referred to above and to assess the impact of tumor infiltration of immune populations and of Cancer-Testis Antigens on tumor behavior and clinical outcomes. Another of the OCC's projects, the "CHIC-STSO1" trial, has been awarded a PHRC-K 2018 grant. Coordinated by Dr. T. Valentin, CHIC-STSO1 will assess the efficacy of perioperative chemotherapy in patients with localized grade-1 or grade-2 soft tissue sarcomas and who are defined as high risk by the CINSARC signature.

• GROUPOS/GSF-GETO project

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 resection reports for bone tumors 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 resection margins of bone sarcomas treated using neoadjuvant chemotherapy.

Main collaborations: links with the ONCOSARC team (CRCT team 19 – Dr. F. Chibon)

Selected publications in 2018:

- . Gelderblom, H. et al. Nilotinib in locally advanced pigmented villonodular synovitis: a multicentre, open-label, single-arm, phase 2 trial. *Lancet Oncol.* (2018).
- . Le Guellec, S. et al. Validation of the Complexity INdex in SARCOMas prognostic signature on formalin-fixed, paraffin-embedded, soft tissue sarcomas. *Ann. Oncol.* (2018).
- . 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.* (2018).

IUCT-O OCC: HEMATOLOGY

Coordinator: Prof. Christian RÉCHER

Type of graft	N° of hospital stays (change compared with 2017)
Total	190 (-3.06%)
Allogeneic transplants	65 (+3.17%)
Autologous transplants	125 (-6.01%)

14 physicians
13,895 hospital stays (+0.55% compared with 2017)
1,533 patients (+1.19% compared with 2017)
10,399 consultations (+3.7% compared with 2017)
57 active trials, including 9 early phase trials

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 national referral center

The OCC is a member of several French networks: IFM, FILO, fi-LMC/GRAALL, FIM, SFGM-TC and LYSA. It is also the hematology referral center for the Occitanie-Pyrénées region and, in conjunction with the Occitanie-Méditerranée referral center, it is drawing up regional guidelines for treating non-Hodgkin lymphomas (NHL).

• JACIE accreditation

2018 saw the OCC take the first 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 covers every aspect of hematopoietic stem-cell transplantation. Its aim is to promote high standards of quality and good practices in the field of hematopoietic cell transplantation and cell therapy. The IUCT-Oncopole's transplantation service and operating suite, and the EFS's cytopheresis facility were audited in November 2018. The results of this audit will be known before the summer of 2019.

• Preparations for major projects in 2019

The arrival of CAR-T cells

CAR-T cells are T lymphocytes taken from patients and then genetically modified in vitro so they express an artificial, or chimeric, antigen receptor. This receptor is designed so its extracellular part recognizes a tumor antigen. Preparations for introducing this innovative

technology, scheduled for 2019, began in 2018.

Extension to the hospitalization department

In the light of the region's growing population (Occitanie is France's second-fastest growing region) and changes in society's needs, and in order to ensure patients have access to novel therapies, the hematology hospitalization department is expanding. Approval has been given to open an extra 15 beds.

• Hematology care pathways training day

At the initiative of D. Yerle, a nurse in the hematology and internal medicine departments who specializes in complex care pathways, in 2014 the IUCT-Oncopole began organizing a regional Hematology Care Pathways symposium. As well as providing an interdisciplinary and inter-professional discussion forum, this bi-annual event helps improve both networking within the area and the transfer of expertise from the hospital to other healthcare professionals.

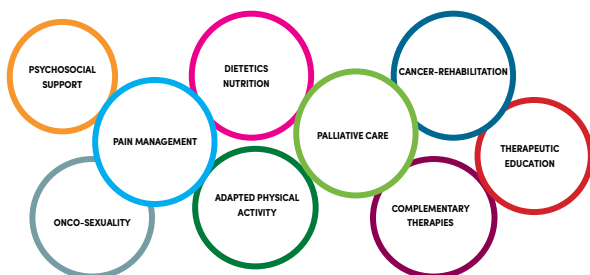
Main collaborations: CRCT teams 8 (Dr. S. Manenti), 9 (Dr. J.-J. Fournié), 12 (Dr. M. Poirot & Dr. S. Silvente-Poirot), 13 (Prof. H. Avet-Loiseau & Dr. L. Martinet), 16 (Prof. E. Delabesse) and 18 (Dr. J.-E. Sarry)

Selected publications in 2018:

- . Bertoli, S. et al. Dexamethasone in hyperleukocytic acute myeloid leukemia. *Haematologica* (2018).
- . Gay, F. et al. Maintenance Treatment and Survival in Patients With Myeloma: A Systematic Review and Network Meta-analysis. *JAMA Oncol* (2018).
- . Huguet, F. et al. Intensified Therapy of Acute Lymphoblastic Leukemia in Adults: Report of the Randomized GRAALL-2005 Clinical Trial. *J. Clin. Oncol.* JCO2017768192 (2018).

IUCT-O OCC: SUPPORTIVE CARE (DISSPO)

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



64 members, including 10 physicians and 12 external practitioners
112,332 patients (+18.83% / 2017)
45,626 procedures (+8.32% / 2017), an average of 3.7 procedures per patient

36% of all patients treated, including all inpatients, treated received at least one form of supportive care

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

• Regional referral center for therapeutic education

In 2018, Occitanie Regional Health Agency asked the IUCT-Oncopole to coordinate 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

“OFF, l'autre séance”: These monthly gatherings centered round a film show allow young patients (AYA – 15–25 years old) to share experiences and obtain support.

Supporter Tour: The IUCT-Oncopole hosted the “Grand Départ” of the AFSOS's (Francophone Association for Cancer Supportive Care) Supportive Care Tour de France, which began on March 21, 2018. The event was designed to raise awareness of the different types of supportive care available and provide information to patients and their families.

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

Conference on caregivers: In order to celebrate the Palliative Care Association's (ASP) 30th anniversary, the OCC helped organize a week of events on the theme of caregivers.

• Sport & Cancer Center

The IUCT-Oncopole's Sport & Cancer Center enables cancer patients to take part, free of charge, in adapted

physical activity sessions. Inaugurated in 2017, it is one of eight such centers funded by CAMI Sport & Cancer and its partners across France. Stade Toulousain Rugby Club began contributing to the program in 2018 by providing sports therapy sessions at the Ernest-Wallon Stadium.

• Focus on palliative care

Palliative care is a central issue for the OCC, which invited Prof. Colombat (Tours University Hospital), to run a training day on the “participative approach”. The physicians and healthcare managers who attended the workshop learnt how this approach can help prevent burnout among professionals. A number of research projects on palliative care are ongoing.

• New research projects for 2018

Three projects received funding in 2018. **RUGBI** (ANR): Search for Relevant Language Units to Improve the Measure of Intelligibility of Speech Marked by Pathological Disorders – **EXPERTISS** (INCa): development of multiple skills to reduce social inequalities in health – **E-POPEE** (Ligue Contre le Cancer): impact of sexuality consultations on the quality of life of patients receiving brachytherapy.

Main collaborations: IFERISS-CRESCO (Prof. T. Lang) and Canadian Institutes of Health Research–Léa Roback Center (Dr. M-F. Raynault)

Selected publication in 2018:

Fujiso, Y. et al. Swall-E: A robotic in-vitro simulation of human swallowing. PLoS ONE 13, e0208193 (2018).

IUCT-O OCC: HEAD AND NECK CANCERS

Coordinators: Prof. Sébastien VERGEZ and Dr. Michel RIVES

Activity	Active files (change compared with 2017)
Total	739 (+8.52%)
Surgery	222 (+18.72%)
Chemotherapy	283 (+13.20%)
Radiotherapy	323 (+9.12%)

15 physicians
10,482 hospital stays (+13.04% compared with 2017)
739 patients (+8.52% compared with 2017)
7,369 consultations (+3.5% compared with 2017)
12 trials open, including 2 phase 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 increasing the number of trials it runs, sponsoring more trials and conducting clinical trials in every area of its activities.

• Regional referral center

Thanks to its expertise in anatomopathology and sinus, cranial base and salivary gland surgery, the IUCT-Oncopole has been designated a regional referral center for rare head and neck cancers. The Head and Neck OCC is currently working with the Onco-Occitanie network, Toulouse University Hospital (at Larrey and Purpan) and the Clinique Pasteur to update regional treatment guidelines.

• Remodeling of the operating suite reception area

The reception area was remodeled in 2018 to make the operative suite more comfortable for ambulatory patients. In consultation with users' representatives, the reception area has been redesigned to include a waiting room with TV, a consultation room for surgeons and anesthetists, and a transfer area for bed patients. This remodeling is part of a larger plan to expand outpatient surgery.

• Knowledge sharing

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

• First trial dedicated to 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. Coordinated by Dr. A. Modesto,

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 devoted to patients with a virus-associated cancer of the oropharynx.

Inclusions have begun and will continue until the end of 2020. An immune-monitoring study will be carried out in parallel in collaboration with CRCT team 1 (Prof. M. Ayyoub).

• 3D printing aids bone reconstruction

Close collaborations with CIRIMATR and Anatomik-Modeling have enabled the development of 3D-printing techniques for producing custom-cutting guides and mandible and maxilla phantoms. These techniques not only substantially reduce surgery times (by about 2 hours on average), thereby improving the survival of bone grafts, they also produce better morphological and functional results.

Main collaborations: CRCT team 9 (Dr. J.-J. Fournié) and the CIRIMAT Laboratory (UMR CNRS INPT UPS 5085 – Prof. C. Laurent).

Selected publications in 2018:

- . Mazerolle, P. et al. Oncological and functional outcomes of trans-oral robotic surgery for pyriform sinus carcinoma: A French GETTEC group study. *Oral Oncol.* 86, 165–170 (2018).
- . Tao, Y. et al. Randomized trial comparing two methods of re-irradiation after salvage surgery in head and neck squamous cell carcinoma: Once daily split-course radiotherapy with concomitant chemotherapy or twice daily radiotherapy with cetuximab. *Radiother Oncol* (2018).
- . Siu, L. L. et al. 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* (2018).

IUCT-O OCC: NEURO-ONCOLOGY

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

Activity	Active files (change compared with 2017)
Total	298 (+0.34%)
Chemotherapy	162 (+5.88%)
Radiotherapy	166 (-9.29%)

7 physicians
5,019 hospital stays (-11.85% compared with 2017)
298 patients (+0.34% compared with 2017)
995 consultations (+20.25% compared with 2017)
9 trials open, including 4 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, as well as metabolic imaging for predicting responses to radiotherapy and for monitoring radiotherapy-chemotherapy combinations.

• Increasing clinical activity

The OCC's clinical activity has doubled in two years, with 1,117 chemotherapy sessions (for 160 patients) in 2018, compared with 532 sessions in 2016 (excluding clinical trials).

• International case review center

Thanks to the numerous innovative clinical trials it sponsors or takes part in, especially phase I trials of targeted therapies, the IUCT-Oncopole has become an international neuro-oncology case review center. The CCO is also a regional case review center for reirradiation following immunotherapy.

• Member of leading networks

Prof. E. Moyal became a member of the European Association of Neuro-Oncology's (EANO) Scientific Committee in 2018 and will therefore help draw up the program for the next annual congress, in Lyon in 2019. 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.

• Discovery of three genes that predict radiosensitivity

Analysis 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 three-gene signature that can be used to predict the radiosensitivity of patients with high-grade oligodendrogliomas. These results will be presented at ASCO 2019.

• Collaboration with Spain's National Cancer Research Center (CNIO)

Prof. E. Moyal is the co-coordinator of the "S100A9-dependent radiation resistance in brain metastasis" project, alongside Dr. M. Valiente at the CNIO in Madrid. In 2018, this project was awarded international funding from Worldwide Cancer Research, a UK cancer research charity.

• SIGN'IT funding for the S12GMA project

Funding for the S12GMA (Stereotactic Irradiation and Immunotherapy Glioblastoma Markers) project was obtained via the ARC's first SIGN'IT call for proposals. Designed to build on data obtained during the STE-RIMGLI phase I-II trial (study of combined hypo-fractionated stereotactic radiation therapy and the anti-PDL1 Durvalumab in patients with recurrent glioblastoma), the project is the fruit of a collaboration between the Department of Radiotherapy and Medical Physics, the Oncogenetics Laboratory, the Pathology Department, CRCT teams 1 and 11, and Grenoble Institute of Neurosciences. It will be launched in 2019 and will be coordinated by Prof. E. Moyal.

Main collaborations: CRCT team 11 (Prof. E. Moyal & Dr. C. Toulas) and Inserm ToNIC Unit team 1 (Dr. P. Péran)

Selected publications in 2018:

- . Kowalski-Chauvel, A. et al. Alpha-6 integrin promotes radioresistance of glioblastoma by modulating DNA damage response and the transcription factor Zeb1. *Cell Death Dis* 9, 872 (2018).
- . Rudà, R. et al. EANO guidelines for the diagnosis and treatment of ependymal tumors. *Neuro-oncology* 20, 445–456 (2018).
- . Siegfried, A. et al. EWSR1-PATZ1 gene fusion may define a new glioneuronal tumor entity. *Brain Pathol.* (2018).

IUCT-O OCC: ONCOGENETICS

Coordinators: Prof. Rosine GUIMBAUD and Dr. Vivian FEILLEL

Number of consultations	
1 st for a relative	430
1 st for an index case	661
Support and/or communication of results	1,003

6 physicians
2,828 consultations in 2018, including 2,094 consultations at the IUCT-Oncopole
4 clinical trials dedicated to oncogenetics

Strategic objectives: The Oncogenetics OCC's main goal is to respond to changing needs in order to ensure it continues to meet 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.

• Regional coordination to optimize support for patients

The Oncogenetics OCC coordinates the four genetic testing centers in the Occitanie-Ouest region (IUCT-Oncopole, Clinique Pasteur, Clinique de l'Ormeau and Rodez hospital). It organizes weekly regional MDT meetings and, in 2018, began setting up an inter-regional polyposis MDT based on videoconference meetings with the teams in Montpellier. 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 specific monitoring programs for three conditions (breast-ovarian cancer syndrome, Lynch syndrome, familial adenomatous polyposis).

• Active member of the GENEPEY network

GENEPEY is a regional oncogenetics network that was set up at the initiative of the IUCT-Oncopole, the Clinique Pasteur and the Onco-Occitanie regional cancer network in order to improve support for individuals with a hereditary predisposition to breast and ovarian cancers or to colorectal and endometrial cancers. GENEPEY, which is run by the Oncogenetics OCC, facilitates and coordinates the provision of optimal care, taking into account INCa recommendations. It is based on collaboration between oncogenetics consultants and other healthcare professionals in public institutions, private establishments or private practice (family practitioners, gynecologists, surgeons, radiologists, oncologists, gastroenterologists, psychologists, etc.) who wish to contribute to the monitoring of people

with a hereditary predisposition to cancer. The network ensures homogenous medical discourse between all the people involved.

• BRCA Café

BRCA Café is the name given to a novel form of discussion group for women with a hereditary predisposition to breast and ovarian cancer. Launched by the OCC in 2018 and coordinated by J. Grondin through the GENEPEY network, the bi-monthly BRCA Café get-togethers are designed to create a warm, friendly and confidential atmosphere in which women can discuss a variety of themes, including risk, prophylactic surgery and transmission. BRCA Café sessions are co-run by a person with a hereditary predisposition to cancer and held at "La Part du Hasard", an arts café in the center of Toulouse. They are open to all women with a BRCA 1 or BRCA 2 genetic mutation, although each group is limited to 10 participants in order to facilitate discussion.

Main collaborations: CRCT team 2 (Dr. J.-S. Hoffmann)

Selected publication in 2018 :

. 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* (2018).

IUCT-O OCC: SKIN CANCERS

Coordinators: Prof. Nicolas MEYER and Dr. Dimitri GANGLOFF

Activity	Active files (change compared with 2017)
Total	665 (+16.26%), including 436 for melanomas (+33.4%)
Surgery	381 (+10.76%), including 239 for melanomas (+9.13%)
Chemotherapy	233 (+30.9%), including 190 for melanomas (+33.8%)
Radiotherapy	117 (+2.63%), including 56 for melanomas (+33.3%)

21 physicians

4,225 hospital stays (+11.92% compared with 2017), including 2,620 for melanomas (+33.4%)

665 patients (+16.26% compared with 2017), including 436 for melanomas (+33.4%)

6,798 consultations (+8.8% compared with 2017), including 2,140 for melanomas (+1.5%)

20 clinical trials ongoing, including 4 phase I-I/II trials

Strategic objectives: The OCC is one of only a few entities in France with the expertise to treat all neoplastic diseases. Its medical objectives are to expand its use of Mohs micrographic surgery¹ under local and regional anesthetic, to expand its role as a referral center for cutaneous imaging of skin cancers, and to create a specific immuno-oncology unit. In terms of research, our objectives focus on prognostic biomarkers, the monitoring of metastatic patients, and BRAF V600 inhibitor resistance mechanisms.

• National referral center

The IUCT-Oncopole has been a member of the INCa-accredited CARADERM network of rare skin cancer centers since 2017. In addition, in 2018, Dr. C. Pages coordinated the drafting of treatment guidelines for Kaposi's sarcoma and Dr. K. Kolsi carried out the first ganglion transfer surgery at the IUCT-Oncopole, making it one of only three centers in France to provide this innovative corrective procedure for refractory lymphedema.

• Introduction of a systematic adjuvant treatment

2018 saw the introduction (excluding clinical trials) of targeted therapy as a systematic adjuvant treatment for melanomas that have reached the lymph nodes. This new approach is part of a move away from surgery to medical therapies and will lead to the reorganization of melanoma treatment at the IUCT-Oncopole.

• Recognized expertise in treating undesirable side effects

The IUCT-Oncopole is internationally known for its expertise in the dermatological toxicity of cancer treatments and trains numerous healthcare professionals from all around the world. In 2018, at the initiative of Dr. V. Sibaud, work began on creating a European dermatological toxicity network.

• Deployment of immunotherapy

First used to treat melanomas, immunotherapy is now being applied to advanced squamous cell carcinomas

and Merkel cell carcinoma. This development led the Department of Internal Medicine to set up an "Immunotherapy Toxicity" MDT at the end of 2017. A major research focus for 2018, in view of the new guidelines being drawn up by the ESMO, was to characterize toxicities linked to immunotherapies.

• Access to innovation

The OCC coordinates or contributes to numerous clinical trials. NEKTAR and BOOSTER MELANOMA were two of the most notable trials to recruit their first patients in 2018. NEKTAR will evaluate a "new generation" immunotherapy in which a CD122-biased agonist is used to selectively increase anti-cancer T cells and "natural killer" cells in the tumor microenvironment and increase the expression of PD-1 in immune cells. BOOSTER MELANOMA will evaluate a new treatment for melanoma based on combining a pair of immunotherapies (Ipilimumab + Nivolumab) with radiotherapy.

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

Selected publications in 2018:

- . Dupuis, F. et al. Clinical, histological and molecular predictors of metastatic melanoma responses to anti-PD-1 immunotherapy. *Br. J. Cancer* (2018).
- . Garandeau, D. et al. Targeting the sphingosine 1-phosphate axis exerts potent antitumor activity in BRAF^{v600}-resistant melanomas. *Mol. Cancer Ther.* (2018).
- . Pascal, P., Derclé, L., Weyts, K., Meyer, N. & Courbon, F. Complete Metabolic Response of Advanced Melanoma to Vemurafenib Assessed with FDG-PET-CT at 85 Hours. *Clin Nucl Med* 43, 333–334 (2018).

(1) Micrographic surgery associates microscope analyses of the whole excision piece with a map showing the position of the tumor in frozen sections, obtained within an hour of obtaining the excision. This method reduces excision margins and ensures complete removal of the tumor.

IUCT-O OCC: ONCOGERIATRICS

Coordinators: Dr. Loïc MOUREY and Dr. Laurent BALARDY

Indicator	N° of evaluations
Mobile oncogeriatrics team (EMOG)	1,280
Registered nurse	200

6 physicians
2 clinical trials dedicated to over-75s in 2018 and another 119 trials open to patients aged 75 years or older

Strategic objectives: The Oncogeriatrics OCC meets the needs of older patients at all three IUCT sites by ensuring they have access to the most appropriate care and the most innovative therapies, wherever they first received treatment. It also addresses future challenges in oncogeriatrics by sponsoring research projects such as the ongoing regional PHRC FRACTION project (to predict the toxicity of chemotherapy as a function of bodily composition).

• Coordinated care across the region

The IUCT-Oncopole's Oncogeriatrics OCC collaborates closely with Toulouse University Hospital's Geriatric Medicine Department via the Regional Coordination Unit for Oncogeriatrics (UCOG), which was set up in 2006 in conjunction with the Onco-Occitanie regional cancer network. This INCa-approved unit ensures that all older patients with cancer obtain appropriate care and sponsors clinical research in the field. A mobile oncogeriatrics team (EMOG) provides specialist expertise to the IUCT-Oncopole's different departments and other hospitals in the region.

• National recognition for oncogeriatrics research

In 2018, Dr. L. Mourey succeeded Dr. E. Brain (Institut Curie) as president of GERICO, a cooperative group of oncogeriatrics specialists that was launched by UNICANCER in 2002. GERICO's members work together to promote clinical research and innovation in oncogeriatrics, focusing especially on developing new types of therapeutic trials specifically aimed at older patients, mainly by adapting methodologies and rationalizing diagnoses and treatments.

• A statistical tool particularly suited to clinical trials involving older patients

As part of a project funded by the Ligue Contre le Cancer, a team of cancer specialists and biostatisticians from the IUCT-Oncopole, in collaboration with researchers from the Institut Curie (Paris) and Institut Paoli-Calmettes (Marseille), has compared different trial designs capable of taking into account heterogeneity within sample populations. According to their results, adaptive methodologies can be used to identify subgroups of patients who benefited, or not, from a therapy, without substantially increasing the number of participants needed (which would reduce a study's feasibility). In order to encourage the scientific community to use these methodologies, the team has created a free software package (R package) that can be downloaded from the CRAN network's website.

Main collaborations: The Oncogeriatrics OCC is a collaborative body that brings together Toulouse University Hospital's Department of Geriatric Medicine and the IUCT-Oncopole's oncogeriatrics team.

Selected publications in 2018:

- . Berbon, C. et al. [Nurse telephone follow-up, a beneficial tool in geriatric oncology]. *Rev Infirm* 67, 37–38 (2018).
- . Cabarro, B. et al. Addressing heterogeneity in the design of phase II clinical trials in geriatric oncology. *Eur. J. Cancer* 103, 120–126 (2018).
- . Capucine, B., Loic, M. & Gabor, L. Perspectives on geriatric oncology research presented at the 2018 European Society for Medical Oncology: Young international society of geriatric oncology report. *J. Geriatr Oncol* (2018).

IUCT-O OCC: THYROID AND NEUROENDOCRINE CANCERS

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

Activity	Active files
Total	526
Surgery	54
Chemotherapy	32
Radiotherapy	316
Brachytherapy	71

22 physicians
766 hospital stays:¹
1,251 consultations (+180)
7 clinical trials ongoing, including 1 phase I prospective trial

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

• A specific structure

Thyroid diseases bring together Toulouse University Hospital's endocrinology, head and neck surgery and thoracic surgery departments, and the IUCT-Oncopole's nuclear medicine and head and neck surgery departments.

Neuroendocrine tumors bring together several departments at the IUCT-Rangueil-Larrey (PHU-MAD:² 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 TEN-GEN network, advises the OCC on endocrine tumor molecular biology.

• National and international 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). In addition, Dr. S. Zerdoud is a member of the European Association of Nuclear Medicine's (EANM) Thyroid Committee.

At the Purpan site's expertise in treating endo-

crine tumors, the OCC is working in conjunction with the Medical Imaging Department to obtain European NeuroEndocrine Tumor Society (ENETS) accreditation.

• Specialist MDTs

The OCC holds specialist MDT meetings on several themes: a neuroendocrine tumors MDT meeting every two weeks (RENATEN review MDT, Prof. R. Guimbaud), a neuroendocrine tumor molecular biology MDT meeting every two months, held in conjunction with the Institut Fédératif de Biologie (Prof. F. Savagner), and three thyroid MDT meetings (Dr. S. Zerdoud) every month, including a standard meeting every week and two review meetings (a bi-weekly national TUTHYREF meeting and a monthly regional metastatic tumors review MDT meeting).

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

Selected publications in 2018:

- . Dumont, S. et al. Transcriptional orchestration of mitochondrial homeostasis in a cellular model of PGC-1-related coactivator-dependent thyroid tumor. *Oncotarget* 9, 15883–15894 (2018).
- . Puzkiel, A. et al. Evaluation of the Interaction of Amino Acid Infusion on 177Lu-Dotatate Pharmacokinetics in Patients with Gastroenteropancreatic Neuroendocrine Tumors. *Clin Pharmacokinet* (2018).
- . Salazar, R. et al. Phase II Study of BEZ235 versus Everolimus in Patients with Mammalian Target of Rapamycin Inhibitor-Naïve Advanced Pancreatic Neuroendocrine Tumors. *Oncologist* 23, 766–e90 (2018).
- . Schlumberger, M. et al. Outcome after ablation in patients with low-risk thyroid cancer (ESTIMABL1): 5-year follow-up results of a randomised, phase 3, equivalence trial. *Lancet Diabetes Endocrinol* (2018).

(1) Solely for thyroid cancers: official statistics do not allow figures for neuroendocrine cancer to be extracted separately.

(2) PHU-MAD = University Hospital Center for Diseases of the Digestive System.

IUCT-O OCC: UROLOGY

Coordinators: Prof. Bernard MALAUAUD, Dr. Loïc MOUREY and Dr. Pierre GRAF-CAILLEAUD

Activity	Active files (change compared with 2017)
Total	888 (-3.37%)
Surgery	101 (-0.98%)
Chemotherapy	308 (-7.78%)
Radiotherapy	334 (0%)
Brachytherapy	64 (0%)
Bladder instillation	61 (+16.39%)

17 physicians
11,419 hospital stays (+1.99% compared with 2017)
888 patients (-3.37% compared with 2017)
4,411 consultations (+8.9% compared with 2017)
33 clinical trials open, including 4 phase I-I/II trials

Strategic objectives: The Urology 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).

• Internationally recognized expertise

The Urology OCC is a world pioneer in en-bloc endoscopic resection of bladder tumors. Thanks to a partnership with Olympus, the IUCT-Oncopole has state-of-the-art equipment and regularly organizes training sessions that attract surgeons from throughout Europe.

• INCa-accredited referral center

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

• Innovation at the heart of patient care

In order to define the optimum treatment options for localized prostate cancer, transrectal or transperineal multi-parametric-MRI guided (KOELIS system) biopsies are performed for most patients.

In addition, as one of the few units in France to carry out 3rd-generation remedial cryotherapy, the OCC attracts patients from throughout the country.

Finally, 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.

Main collaborations: "Sphingolipids and Cancers" team at the CNRS Institute of Pharmacology and Structural Biology (IPBS, Dr. O. Cuvillier)

Selected publications in 2018:

- . Covin, B. et al. Refining the risk-stratification of transrectal biopsy-detected prostate cancer by elastic fusion registration transperineal biopsies. *World J Urol* (2018).
- . Graff, P. et al. IDEAL 2a Phase II Study of Ultrafocal Brachytherapy for Low- and Intermediate-risk Prostate Cancer. *Int. J. Radiat. Oncol. Biol. Phys.* (2018).
- Overs, C. et al. Robot-assisted post-chemotherapy retroperitoneal lymph node dissection in germ cell tumor: is the single-docking with lateral approach relevant? *World J Urol* 36, 655–661 (2018).

DEPARTMENT OF INTERNAL MEDICINE

Coordinator: Prof. Odile BEYNE-RAUZY

6 physicians

34,383 hospital stays (+10% compared with 2017), 81.6% of which were day hospital stays

Active files: 892 patients (+4.5% compared with 2017)

2,186 consultations (+6.9% compared with 2017)

1,692 LBP transfusion sessions (+3.4% compared with 2017)

462 non-scheduled acute cases treated (12.9% of outpatient cases)

19 clinical trials open, 11 of which were active (44 inclusions) in 2018

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, represented by Prof. Daniel Adoue, is one of four national referral centers for autoimmune cytopenia in adults (CeRe-CAI). 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. Comont)

Manage complex pathways (D. Yerle).

• Creation of an immunotherapy toxicity MDT

Multidisciplinary and multi-organ MDT review meetings focusing on immunotherapy toxicities have been held every month since 2017. Organized in conjunction with the Onco-Occitanie network and coordinated by Dr. T. Comont, they are open to all prescribing physicians in the Occitanie region, who can join meetings by videoconference. They address three essential issues: treating severe toxicities, re-administering an immunotherapy following the appearance of undesirable side effects and administering immunotherapy to patients who suffer from an autoimmune disease.

• The Complex pathways nurse – a key player in the process

Complex pathways nurse is a new specialty at the crossroads between internal medicine and hematology. These specialist nurses provide support for medical and paramedical teams by coordinating and organizing complex pathways, and by supporting patients and other healthcare professionals involved in the treatment. In 2018, 77 patients, including 56 new patients, benefited from this support. This innovative approach facilitates networking across the region and promotes the transfer of competencies to local healthcare professionals. Creating this post has also helped shorten hospital stays in the department.

• End of inclusions for two promising trials

Recruitment for the PREDICTOR and LUSPATERCEPT trials ended in 2018. PREDICTOR, conducted in collaboration with the mobile oncogeriatrics unit, was designed to determine the best overall-survival predictive marker for older patients with high-grade myelodysplastic syndromes (trial sponsored by INCa). LUSPATERCEPT was an international trial focusing on myelodysplastic anemia. Results from both trials will be published in 2019.

Main collaboration: CRCT team 18 (Dr. J-E. Sarry)

Selected publications in 2018:

- . Comont, T., Sibaud, V., Mourey, L., Cougoul, P. & Beyne-Rauzy, O. Immune checkpoint inhibitor-related acral vasculitis. *J Immunother Cancer* 6, 120 (2018).
- . Essilini, A. et al. Pretreatment with standard-dose intravenous methylprednisolone does not improve outcomes in newly diagnosed immune thrombocytopenia (ITP). *Eur. J. Haematol.* 100, 412–418 (2018).
- . Vaysse, C. et al. The Impact of a Small Private Online Course as a New Approach to Teaching Oncology: Development and Evaluation. *JMIR Med Educ* 4, e6 (2018).

ASSOCIATED OCC: DIGESTIVE CANCERS

Coordinator: Prof. Rosine GUIMBAUD

Activity	Active files (change compared with 2017)
Total	2,630 patients (-2.56%)
Surgery	887 patients (-2.74%)
Chemotherapy	50 patients (-4.63%)
Radiotherapy	238 patients (-0.83%)
Brachytherapy	2 patients (-71.43%)

14 physicians
12,567 hospital stays (-5.08% compared with 2017)
Collaborations with CRCT teams 2 (Dr. J-S. Hoffmann) and 10 (Dr. P. Cordelier)

Strategic objectives: The Digestive Cancers OCC works closely with the IUCT-Rangueil/Larrey's digestive cancers teams in order to treat all forms of digestive cancer: colorectal, pancreatic, esophageal, stomach, etc.

In addition to its clinical activities, the OCC contributes to several research projects, generally in collaboration with CRCT teams 2 (Dr. J-S. Hoffmann) and 10 (Dr. P. Cordelier) and aimed at developing innovative therapies for digestive cancers, especially pancreatic cancer and colorectal cancer.

Selected publication in 2018:

. Lièvre, A. et al. Correction: Protein biomarkers predictive for response to anti-EGFR treatment in RAS wild-type metastatic colorectal carcinoma. Br. J. Cancer (2018).

ASSOCIATED OCC: THORACIC CANCERS

Coordinator: Prof. Julien MAZIÈRES

Activity	Active files (change compared with 2017)
Total	1,784 patients (+4.02%)
Surgery	57 patients (+5.79%)
Chemotherapy	621 patients (+2.8%)
Radiotherapy	379 patients (-7.11%)

5 physicians
12,328 hospital stays (-1.59% compared with 2017)
450 new lung cancer patients (180 early stage and 270 advanced stage), **15 mesotheliomas and 15 thymomas**
23 clinical trials ongoing (220 patients included)
Collaborations with CRCT teams 1 (Prof. M. Ayyoub), 3 (Prof. G. Favre) and 20 (Dr. S. Valitutti)

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, markers of bronchial cancers in women and toxicity management.

In 2018, the LUNG-RESIST project, whose purpose is to understand and overcome adaptive resistance to tyrosine-kinase EGFR in lung cancer, was awarded grants for its two components: a PRTK-2018 grant and an @IUCT-O translational research grant.

The "LUNG-PREDICT" project was also launched in 2018, in collaboration with Laboratoires Pierre Fabre. Its aim is to create clinical-biological databases for use in molecular MDT meetings.

Selected publication in 2018:

. Gandara, D. R. et al. Atezolizumab Treatment Beyond Progression in Advanced NSCLC: Results From the Randomized, Phase III OAK Study. *J Thorac Oncol* 13, 1906–1918 (2018).

ASSOCIATED OCC: PEDIATRIC ONCOLOGY

The Pediatric Oncology OCC was created in 2018 as the culmination of a long-standing arrangement by 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 Renaud (radiotherapy and nuclear medicine teams).

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

Activity	Active files
Total	457 patients
Surgery	114 patients
Chemotherapy	170 patients
Radiotherapy	35 patients

15 physicians
3,437 hospital stays
1,905 consultations
108 clinical trials open in 2018
Collaborations with CRCT team 1 (Prof. E. Delabesse) and the DEVIN team (Dr. P. Péran) at UMR Inserm 1214

Strategic objectives: The main objectives for 2019 will be to finalize the JACIE accreditation procedure, obtain a biomedical research authorization for the pediatric onco-hematology unit and extend the Langlade BRL's nuclear medicine authorization to children. Treating AYA cancer patients also requires the Pediatric Oncology OCC to coordinate with the other OCCs. A registered nurse and an educator have been appointed to organize this treatment sector, which lies at the interface between pediatrics and adult hemato-oncology (AJAMIP network). Another objective is to increase inclusions in early phase clinical trials run at the different sites. Doing so will strengthen the IUCT-Oncopole's application to renew its early phase trials center (CLIP²) accreditation.

. Members of the OCC help run 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. A coordinating nurse organizes patient care within the inter-regional healthcare sector. Several members of the OCC belong to the French Children's Cancers Society (SFCE) and are involved in national and international organ committees. Dr A. Bertozzi is a member of the SFCE's board and Prof. A. Laprie is a member of its scientific council.

. In terms of basic research, the OCC focuses on two

main themes within the Integrated Research Actions Program (PAIR):

- "Brain tumors, biologics and cognition" (in collaboration with the Neuro-oncology OCC and the DEVIN team at the Inserm 1214 ToNIC UMR.)

- "Connect AML" (Dr. M. Pasquet, pediatrician, oncologist and member of CRCT team 16).

Selected publication in 2018:

. Ducassou, A. et al. Pediatric Localized Intracranial Ependymomas: A Multicenter Analysis of the Société Française de lutte contre les Cancers de l'Enfant (SFCE) from 2000 to 2013. *Int. J. Radiat. Oncol. Biol. Phys.* 102, 166–173 (2018).

Medico-technical services

Twelve medico-technical departments provide support services for the Organ Coordination Committees' patient care and research activities. In addition, they use their cutting-edge facilities to carry out their own research projects.

Medical Imaging Department

Department head: Prof. Frédéric Courbon

Assistant head: Prof. Nicolas Sans

38,016 procedures (+3.4% compared with 2017), including 12,186 nuclear medicine procedures, 9,473 TDM scans, 4,100 MRI scans, 6,447 x-rays, and 2,325 ultrasound scans.

Seven clinical trials open in 2018 (14 inclusions)

- The 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) was launched in 2018 to review processes within the three services and their interactions with the medical physics, hospitalization and radioprotection departments. Holding periodic multidisciplinary meetings ("chats") has helped strengthen cohesion and improved communication.

Moreover, Occitanie Regional Health Agency has provided funding to create a shared patient ID server and thereby strengthen the department's collaborations with the independent sector.

- 2018 saw an ambitious program of investments that included the purchase of a second PET scanner, a stereotactic breast biopsy unit (tomosynthesis, or 3D mammography), and several specialist software packages. In addition, a new type of scanner, currently

under development, will be bought in 2020 in order to continue expanding the department's interventional radiology capabilities.

- A partnership with General Electric was launched in 2018 to develop and evaluate a new generation PET scanner ("PET Concept Car" program).

- The Medical Imaging Department is sponsoring three projects within the ANITI (Artificial and Natural Intelligence Toulouse Institute) program. Sponsored by the Federal University of Toulouse Midi-Pyrenees, ANITI is due to be named one of the ANR's four multidisciplinary institutes for artificial intelligence research (3IA).

- The Medical Imaging Department's PET center has been an EARL/EANM accredited European Center of Excellence since 2015. In addition to recognizing the high quality of the center's patient care and examinations, this accreditation facilitates participation in European research protocols, such as those sponsored or supported by the OERTC. In addition, work is underway to obtain European Neuroendocrine Tumor Society (ENETS) accreditation for the site's expertise in treating endocrine tumors

Selected publications in 2018:

- . Brun, T. et al. New approach of ultra-focal brachytherapy for low- and intermediate-risk prostate cancer with custom-linked I-125 seeds: A feasibility study of optimal dose coverage. *Brachytherapy* (2018).
- . Kanoun, S., Rossi, C. & Casasnovas, O. [18F]FDG-PET/CT in Hodgkin Lymphoma: Current Usefulness and Perspectives. *Cancers (Basel)* 10, (2018).
- . Pascal, P., Dercle, L., Weyts, K., Meyer, N. & Courbon, F. Complete Metabolic Response of Advanced Melanoma to Vemurafenib Assessed with FDG-PET-CT at 85 Hours. *Clin Nucl Med* 43, 333-334 (2018).



Nuclear Medicine and Brachytherapy Hospitalization Unit

Unit head: Prof. Isabelle Berry

199 brachytherapies (+8.74% compared with 2017)

1,139 hospital stays, excluding treatment sessions (694 patients), with 29.2% as outpatients, including 189 brachytherapy stays (-8.79% compared with 2017)

- France's largest vectorized internal radiotherapy unit has 18 individual rooms with video monitoring and background radiation measuring. 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 the needs of radiation protection. With high quality facilities (including a high capacity for decontaminating liquids and solids) and expert staff who are particularly attentive to patient comfort, the unit ensures all its patients receive the best possible care.
- Most referrals to the unit, which is a regional brachytherapy referral center, are 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 since 2017 (72 hospital stays in 2018), following the successful completion of clinical trials, carried out under the impulsion of Dr. L. Dierickx.
- The GENBIOLuNET project, led by Dr. L. Vija Racaru,

involves measuring variability in molecular biomarkers that can be used to characterize radio-nucleotide therapies (Lu-177 DOTATATE) administered to patients with metastatic neuroendocrine tumors of the stomach and lower intestine. The project was awarded a GIRCI-SOHO grant in 2018.

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 (+1.73% compared with 2017)

7,701 operations (+2.06% compared with 2017), 2,645 of which were to fit or remove a port or a CVC (+19.85% compared with 2017).

- The Surgery Department's operating suite has seven operating rooms, two conventional wards (50 beds) and a day surgery ward (15 places). Its objectives include extending outpatient surgery and perfecting surgical techniques and equipment.
- Thanks to a partnership with Olympus, one of the operating rooms is equipped with a 3D imaging system. Other innovative techniques used at the IUCT-Oncopole include robotic surgery, hyperthermic intraperitoneal chemotherapy (HIPEC), 3D-printer-assisted mandibular and maxillary bone reconstruction, preoperative radiotherapy (for breast cancers) and focal cryotherapy (for prostate cancer).
- The operating suite reception area was reorganized in 2018 to make it more comfortable for ambulatory patients. Following consultation with users' representatives, the reception desk has been remodeled to include a waiting room with TV, a consultation room for surgeons and anesthetists, and a transfer area for patients in beds. This reorganization is part of a larger project to expand outpatient surgery.
- In its 2018 survey of French hospitals, Le Point magazine ranked the IUCT-Oncopole 3rd for breast cancer surgery (2nd in 2017), 3rd for head and neck cancer surgery (5th in 2017), 6th for gynecological cancer surgery (10th in 2017) and 9th for skin cancer surgery (20th in 2017).
- In 2018, Drs. C. Martinez Gomez, M.A. Angeles, A. Martinez and G. Ferron produced a series of ten-step

guides to a variety of surgical techniques. Each guide was accompanied by a specially made video illustrating its content. After reviewing these clear and easy-to-follow tools, the Spanish Academy of Medicine and Surgery awarded them its Jose Abril Morales Prize. The series will be continued in 2019.

Anesthesiology Unit

Manager: Dr. Sébastien Pierre

4,588 consultations (-0.8% compared with 2017) and

3,898 patients (-0.3% compared with 2017)

4,868 anesthesia procedures of all kinds except local (+2.03% compared with 2017)

- In addition to providing anesthesiology services to all the Institute'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 morphine-sparing strategies.
- Doctors from all around the world come to the anesthesiology unit to learn these innovative techniques.

Intensive and Intermediate Care

Manager: Dr. Jean Ruiz

12 beds

473 patients and 623 admissions, including 456 from the IUCT-Oncopole (surgery: 49.4%, hematology and internal medicine: 16.9%, medical oncology: 6.9%)

Mean length of stay: 5.79 days (5.82 days in 2017)

"Mieux Vivre en Réanimation" is a continuous improvement program aimed at making the intensive care experience as agreeable as possible for patients. The Intensive and Intermediate Care Department, 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 among 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). In addition, 2018 saw the launch of two projects on pneumocystosis (one with the Hôpital Saint-Louis and the other with the Institut Fédératif de Biologie de Toulouse'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 taken into account 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 900 patients.

Selected publication in 2018:

Bertoli, S. et al. Dexamethasone in hyperleukocytic acute myeloid leukemia. *Hématologica* (2018).

Radiotherapy Department

Head of department: Prof. Elizabeth Moyal

Assistant head: Dr. Michel Rives

58,134 radiotherapy sessions in 2018, 77% of which were IMRT (68.7% dedicated IMRT machine)

36 total body irradiation sessions (+56% compared with 2018)

The radiotherapy department keeps fully up to date

with innovations and evolutions 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 them the option of receiving their treatment under hypnosis.

- The department is also highly involved in clinical research and upstream translational research in radiobiology (close links with CRCT team 11), as well as in metabolic and functional imaging for radiotherapy. Hence, it contributes to several projects coordinated by the OCCs and runs numerous trials and research projects.
- 2018 saw the launch of the MARTA PHRC, a multi-center study led by Dr. C. Massabeau that will assess the value of surgical mastectomy treatment with immediate prosthetic reconstruction for breast cancer patients requiring a tomotherapy adjuvant treatment. In addition, a new PHRC grant was obtained for the BLAD-RDA01 project, led by Dr. J. Khalifa, which evaluates consolidative radiotherapy in patients with a metastatic urothelial carcinoma of the bladder.
- The department (Dr. A. Modesto), in collaboration with the Digestive Cancers OCC and 11 other centers in France, contributes to the ARION phase II trial on associating radiotherapy/chemotherapy with immunotherapy (Durvalumab) for non-resectable esophageal cancer. The study is being carried out under the auspices of the UNICANCER-FFCD Digestive Cancer Research Partnership (PRODIGE). An ancillary study to determine the sensitivity of the microbiota to this

treatment will be conducted in collaboration with CRCT team 11 (Prof. E. Moyal and Dr. C. Toulas).

- GIRAFE is another project that began in 2018. Led by Dr. A. Laprie and run in collaboration with Accuracy, GIRAFE's purpose is to evaluate the RADIXACT deformable delineation tomotherapy tool with the aim of integrating it into routine clinical radiotherapy.
- The Booster Melanoma trial, co-managed with Dr. C. Gomez Roca, included its first patients in 2018. Its purpose is to study the induced immune abscopal effect of stereotactic radiotherapy in melanoma patients. Results should be known in 2024.
- 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.
- Finally, 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 was 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.

Selected publication in 2018:

. Attal, J. et al. Subventricular zone involvement at recurrence is a strong predictive factor of outcome following high grade glioma reirradiation. *J. Neurooncol.* 136, 413–419 (2018).

Pharmacy

Manager: Dr. Jean-Marie Canonge

Assistant manager: Dr. Florent Puisset

France's largest hospital pharmacy in terms of chemotherapy preparations

**118,000 preparations, including 9,000 for clinical trials
47,000 anticancer chemotherapy prescriptions**

- The pharmacy's activity continues to increase, especially with respect to chemotherapy preparations for clinical trials, which doubled between 2017 and 2018.
- Given the growing complementarity between physicians and pharmacists, the pharmacist's role in can-



cer treatment pathways for patients treated at home is currently a major issue. Consequently, work is underway to increase the presence of pharmacists and dispensers in healthcare units.

- Furthermore, June 2018 saw the introduction of a system of pharmaceutical consultations involving a “therapeutic patient education pharmacist” who oversees drug-dose adaptation when a patient is discharged and who is responsible for city-hospital liaison at the beginning of treatment in order to reduce the risk of drug interactions.
- These measures also facilitate the evaluation of drugs in current practice through studies of interactions between drugs and between drugs and diet, as well as the use of pharmacokinetic and pharmacodynamic data to optimize doses, particularly in high-risk patients (transfer of personalization tools developed by research projects).
- Preparatory work for obtaining CAR-T cell certification began in 2018. This work, which has been validated by the Regional Health Agency, should lead to the first patients being treated as early as June 2019.
- Finally, as part of a hospital-university cooperation program, the IUCT-Oncopole’s pharmacy has advised Vietnam’s National Cancer Center on transposing Toulouse’s centralized chemotherapy preparation model to Hanoi. Vietnam’s first centralized unit will open in 2019 thanks to the partnership with Toulouse University Hospital begun in 2015.

Selected publications in 2018:

. Paludetto, M.-N. et al. Metalloporphyrin-Catalyzed Oxidation of Sunitinib and Pazopanib, Two Anticancer Tyrosine Kinase Inhibitors: Evidence for New Potentially Toxic Metabolites. *J. Med. Chem.* 61, 7849–7860 (2018).

. Puisset, F. et al. Safety of oral hydration after cisplatin infusion in an outpatient lung cancer unit. *Support Care Cancer* (2018).

Oncology Medical Biology Laboratory (LBMO)

Manager: Prof. Gilles Favre

784,662 examinations (+6.8% compared with 2017) and 8,401,405 class-B procedures (+3% compared with 2017)

RIHN:¹ Oncogenetics 6,514,360 (+24.6% compared with 2017); Prospective biology 917,900 (+0.9% compared with 2017), other sectors (pharmacology, immune-analyses, biochemistry) 467,950 (+238.5% compared with 2017)

• 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).

• 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, Prof. E. Chatelut: team 14. The LBMO also conducts its own research projects.

• Furthermore, the LBMO contributes to clinical trials, notably through ancillary studies conducted in collaboration with the Clinical Trials Office. In response to the growth of this area of its work, the LBMO set up a new clinical trials section in 2018 and appointed a new member of staff to manage samples taken during clinical trials at the IUCT-Oncopole.

• Current research projects involving the LBMO include PADA-1, a UNICANCER-sponsored study to evaluate the safety and efficacy of a combined chemotherapy-hormone therapy treatment driven by monitoring mutations in the circulating DNA of patients with metastatic breast cancer. This project resulted in the Prospective Biology Unit embracing research methodologies incorporating real-time studies of circulating molecules.

• PHACS, a longitudinal study of relationships between pharmacogenetics, pharmacokinetics and toxicity in breast cancer patients treated with tamoxifen or aromatase inhibitors, was coordinated by the Pharmacology and Oncogenetics & Pharmacogenetics Units. Inclusions ended in 2018 (more than 2,000 patients) and the first results should be published at the beginning of 2019.

• An Immune Monitoring Unit was created in 2017 to support the development of immunotherapies in conjunction with IUCT-Oncopole clinicians. Its main objective is to identify the biological parameters underlying responses to the toxicity of immunotherapies in order to help clinicians prescribe the most appropriate therapies. As well as supervising patients receiving treatment, the unit provides specialist monitoring for immunotherapy clinical trials. For example, the MINER trial, which was launched in 2018 by the IUCT-Oncopole with support from the imCORE network and the MSD Avenir foundation, will monitor immunological mechanisms and biomarkers that can be used to assess the efficacy and toxicity of immunotherapy treatments for different cancers (melanomas, lung cancer, bladder

(1) RIHN: Schedule of reimbursements for innovative biological acts



cancer, head and neck cancers, etc.). The unit intends to begin other trials of its own in 2019, building on research carried out by CRCT team 1.

- Moreover, the LBMO collaborates with a variety of biotechnology start-ups and innovative companies, such as Picometrics and Smartcatch, thereby actively contributing to the development of new approaches and technologies. 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 publications in 2018: • Guibert, N. et al. PD-L1 expression in circulating tumor cells of advanced non-small cell lung cancer patients treated with nivolumab. *Lung Cancer* 120, 108–112 (2018).

- Puszkiel, A. et al. Evaluation of the Interaction of Amino Acid Infusion on 177Lu-Dotatate Pharmacokinetics in Patients with Gastroenteropancreatic Neuroendocrine Tumors. *Clin Pharmacokinet* (2018)

Onco-Hematology Transfer Platform

Manager: Prof. Eric Delabesse
29.8 million procedures

- The Onco-Hematology Transfer Platform has units on all three IUCT sites: Oncopole, Rangueil/Larrey and

Purpan. Three of these units – an automated technical center (Dr. J-B. Rieu), a myeloma genomics unit (Prof. H. Avet-Loiseau) and a hemopathy genetics unit (Prof. V. De Mas) – are on the IUCT-Oncopole site.

All three IUCT-Oncopole units saw an increase in their activity compared with 2017: by 3% for the automated technical center, by 16% for the myeloma genomics unit, and by 22% for the hemopathy genetics unit.

- The platform is helping expand the use of new generation sequencing both in treating hematological malignancies and in analyzing other pathologies.

- As well as being a referrals 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), the platform contributes to numerous registers, observatories, working groups, national biological collections, and research-specific biological collections.

- The platform has an international reputation for its clinical research, especially for the work it carries out in collaboration with CRCT team 4 (Prof. T. Levade and Dr. N. Andrieu). It also works closely with four other CRCT teams: 8 (Dr. S. Manenti), 13 (Prof. H. Avet-Loiseau), 16 (Prof. E. Delabesse) and 18 (Dr. J-E. Sarry).

Selected publication in 2018:

- Bertoli, S. et al. Dexamethasone in hyperleukocytic acute myeloid leukemia. *Hæmatologica* (2018).

Pathology Laboratory

Director: Prof. Pierre Brousset

Assistant directors: Prof. Philippe Rochaix and Prof. Emmanuelle Uro-Coste

60,604 cases, including 22,105 external requests for second opinions

76,904 examinations and 68,096 reports sent to prescribers

469,850 slides read and 253,976 paraffin blocks created, including 52,654 for biopsies

Publications – SIGAPS score: 725

Virtual histopathology, full-slide confocal microscopy, multiplexing, AI, NGS

- The pathology laboratory is divided into five units: conventional histopathology, cytology, immune-histochemistry, molecular biology and imaging.
- A member of the INCa-accredited (since 2010) national network of referrals centers, it is the regional referrals 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. P. Rochaix and 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).
- 2018 saw a substantial increase in the laboratory's activity, most notably the tripling of its capacity to process immunohistochemistry samples, an area in which it has recruited additional staff, including a bioinformatician, a molecular biology engineer, a molecular biology assistant and an immunohistochemistry engineer. Some of its anatomopathologists are based at the IUCT-Purpan and IUCT-Rangueil satellite labs, which specialize in extemporaneous preparations. A remote pathology system enables them to seek second opinions from the IUCT-Oncopole's pathologists.
- An application to extend the LabEx TOUCAN hematopoietic cancer research program was drawn up and submitted in 2018. In its first five years, the program's research teams published 215 papers (with an h-index of 31), filed several patents, created two start-ups, and built stronger links with Laboratoires Pierre Fabre and ROCHE. Extending the program for another five years

would provide funding for developing artificial intelligence systems for the Imaging Unit (€1.5 million) and single-cell sequencing (scrRNA-seq), in conjunction with the CRCT (€1.5 million).

- An agreement signed with Terascop in 2018 will enable the unit to provide anatomopathology expertise to healthcare professionals outside France via telepathology or by performing ancillary tests (immunohistochemistry and molecular tests).
- Finally, in 2018 the Pathology Laboratory began the process of obtaining certification for its molecular biology activities.

Selected publications in 2018:

. Evrard, S. M. et al. Targeted next generation sequencing reveals high mutation frequency of CREBBP, BCL2 and KMT2D in high-grade B-cell lymphoma with MYC and BCL2 and /or BCL6 rearrangements. *Haematologica* (2018).

. Le Guellec, S. et al. Validation of the Complexity INDEX in SARCOMAS prognostic signature on formalin-fixed, paraffin-embedded, soft tissue sarcomas. *Ann. Oncol.* (2018).

. Uro-Coste, E. et al. ETMR-like infantile cerebellar embryonal tumors in the extended morphologic spectrum of DICER1-related tumors. *Acta Neuropathol.* (2018).

Cancer BioBank

Manager: Pr Anne Gomez-Brouchet

270 m2 of dedicated space

33 collections, including 13 Cancer BioBank collections and 20 hosted collections.

67,993 samples from 48,615 patients (tumor and non-tumor samples)

8,316 new samples and 5,213 samples provided to research teams in 2018

- The Cancer-BioBank houses several exemplary, declared and authorized collections, such as the samples collected during the multi-center INCa-BACAP project (pancreatic adenocarcinoma biobank), which were received in 2017.
- 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. Hence, its primary function is to manage biological resources and collections by receiving, conserving, preparing and supplying samples that meet the needs of its users. Biological resources are made available, subject to approval by the Scientific Board, in a variety of forms: frozen (fragments, thin sections, unstained slides), paraffin-embedded (blocks,



unstained slides), other (serums) and extracted DNA/RNA (frozen/ paraffin-embedded).

- The Cancer-BioBank contributed to 75 research projects in 2018, including 53 collaborative projects between the site's partners and several academic and external commercial partners (+26% compared with 2017), and to 22 clinical trials (stable compared with 2017). In 2018, a "tissue block library" was created to meet the needs of researchers and private companies. It currently contains samples of breast, kidney, lung and bowel tumors.
- In 2018, the Cancer-BioBank began annotating its flagship collections, starting with the "bone tumors' collection. This process is the first step in strengthening the biobank's collaboration with CRCT team 19 (Prof. F. Chibon).
- 2018 also saw the Cancer-BioBank launch several new projects in close collaboration with EVOTEC, to which the BioBank will supply fresh tissue samples.

Selected publications in 2018:

- . Siegfried, A. et al. EWSR1-PATZ1 gene fusion may define a new glioneuronal tumor entity. *Brain Pathol.* (2018).
- . Tallegas, M. et al. IDH mutation status in a series of 88 head and neck chondrosarcomas: different profile between tumors of the Skull Base and tumors involving the facial skeleton and the Laryngotracheal tract. *Hum. Pathol.* (2018).

Engineering and Medical Physics Department

Manager: Régis Ferrand

3,475 doses calculated in 2018

4,239 doses measured by the GBM department

- In the autumn of 2018, S. Ken joined the Informatics Research Institute of Toulouse's (IRIT) MINDS team (coMputational imagINg and viSion – manager Dr. A. Basarab) as an associate researcher. His work will focus on developing advanced image analysis and interpretation tools.
- 2018 saw the launch of a collaboration with Brain Lab to carry out a detailed study of the two stereotaxis machines used by its system.
- In another collaboration launched in 2018, the department will work with Siemens and Prof. O. Bieri's chemical biophysics team at the University of Basel (Switzerland) to roll out innovative 4D-MRI sequences.
- Furthermore, Oléa Medical awarded S. Ken an innovation grant to study the use of multimodal imaging in focal treatment of the prostate (definition of margins, etc.).
- The Engineering and Medical Physics Department is involved in the automatic segmentation and radiomics component of the COMPUTREAT 2015-2016 project, steered by Prof. L. Ysebaert.
- The French Medical Physics Society (SFPM) held its 2018 annual congress at the IUCT-Oncopole from June 13-15.
- Finally, in May 2018, the radiology technicians team presented the MY Recordable E-learning tool (MYRE), designed by the department's Dr. L. Simon. With its 200 recorded course modules, online questionnaires and resource database, MYRE will be an invaluable continuous self-training and evaluation tool for the department's radiotherapy technicians. It is based on an initial version created by a radiotherapy manager, P. Daguenel, and three technicians, J-B. Lavielle, F. Carles and L. Milhas.

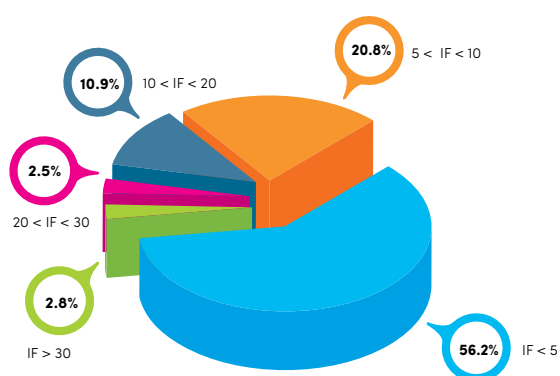


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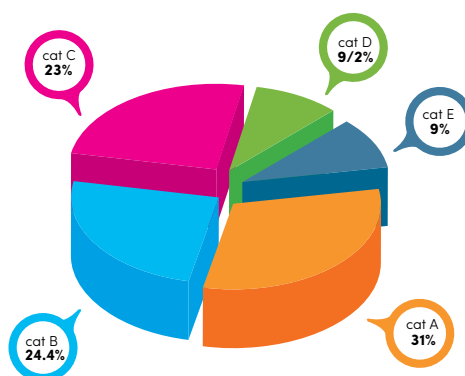
VALORIZATION

Publications

Basic, translational and clinical research activities at the IUCT-Oncopole led to the publication of **568** papers in 2018. These papers were published in **281** journals with a mean impact factor (excluding NR*) of 7.06.



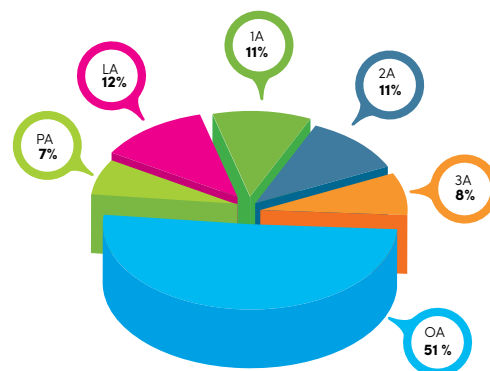
Percentage of papers by impact factor (IF)
- excluding NR*



Percentage of papers by SIGAPS category
- excluding NR*

Top 10 international journals (IF > 10) in which the IUCT-Oncopole published papers in 2018:

1. *Leukemia*
2. *Annals of Oncology*
3. *Blood*
4. *The New England Journal of Medicine*
5. *The Lancet Oncology*
6. *JAMA Oncology*
7. *European Journal of Urology*
8. *Journal of Thoracic Oncology*
9. *Journal of Clinical Oncology*
10. *Clinical Cancer Research*



Percentage of papers by author position
* No SIGAPS ranking

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 by the IUCT-Oncopole in 2018 can be found on our website:

www.iuct-oncopole.fr/publications-scientifiques

In 2018, three IUCT-Oncopole clinicians were invited to join the editorial boards of scientific journals:

- Dr. A. Martinez and Dr. G. Ferron - International Journal of Gynecological Cancer.
 - Dr V. Sibaud - Annales de Dermatologie et de Vénérologie.
- In addition, several of the site's clinicians and researchers have been members of editorial boards for a number of years, inclu-

ding as joint editors (Prof. E. Chatelut: Cancer Chemotherapy and Pharmacology; Prof. C. Laurent: Cancers) or associate editors (Prof. H. Avet-Loiseau: Blood/American Society of Hematology Journal; Dr. C. Bousquet & Dr. S. Pyronnet: Frontiers in Endocrinology; Dr. S. Pyronnet: Cellular Endocrinology Review; Dr. M. Poirot: Frontiers in Oncology/Frontiers in Chemistry/Heliyon; Dr. M. Poirot & Dr. S. Silvente-Poirot: Pharmacologia/Frontiers in Nutrition/Frontiers in Pharmacology; Dr. J. Guillermet: Heliyon; Dr. J Guillermet-Guibert: Plos Genetics; Dr. A. Lemarié: International Journal of Molecular Sciences; Dr. N. Andrieu: American Journal of Cancer Research; L. Astudillo: Médecine Hospitalière).

Patents

15 patent applications were filed in 2018. They are listed below:

Publication n°	Publication date	Title	Applicant
EP3411063	12/12/2018	Methods and pharmaceutical compositions for enhancing cd8+ t cell-dependent immune responses in subjects suffering from cancer	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
EP3407912	05/12/2018	Methods for enhancing the potency of the immune checkpoint inhibitors	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
EP3407911	05/12/2018	Methods and pharmaceutical composition for the treatment of cancer	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
WO2018202850	08/11/2018	Microtubule-targeting drugs as immune checkpoint inhibitors and methods of screening novel immune checkpoint inhibitors for the treatment of cancers and infectious diseases	Inserm, University of Toulouse III–Paul Sabatier, CNRS
WO2018146171	16/08/2018	Methods for treating mast cell activation diseases	Inserm, University of Toulouse III–Paul Sabatier, CNRS, Toulouse University Hospital
WO2018146253	16/08/2018	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
WO2018109146	21/06/2018	Methods and kits for detecting basophil activation	Inserm, University of Toulouse III–Paul Sabatier, CNRS, University of Stanford
EP3314260	02/05/2018	Methods and kits for detecting protein-protein interactions	Inserm, University of Toulouse III–Paul Sabatier
WO2018055080	29/03/2018	Methods and pharmaceutical compositions for re-programming immune environment in a subject in need thereof	Inserm, University of Toulouse III–Paul Sabatier, Affichem
WO2018054960	29/03/2018	Methods for predicting and treating resistance to chemotherapy in npm-alk(+) alcl	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
WO2018046738	15/03/2018	Methods for predicting the survival time of patients suffering from cancer	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
WO2018046736	15/03/2018	Methods for predicting the survival time of patients suffering from cancer	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
WO2018019990	01/02/2018	Methods of treatment of cancer disease by targeting tumor associated macrophage	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital
WO2018020000	01/02/2018	Antibodies targeting tumor associated macrophages and uses thereof	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital, Institut Claude Regaud
WO2018011107	18/01/2018	Use of er-alpha 46 in methods and kits for assessing the status of breast cancer	Inserm, University of Toulouse III–Paul Sabatier, Toulouse University Hospital

Knowledge sharing

1,105 students, including 199 interns and 69 doctoral students

Students from 37 countries

110 IUCT-Oncopole professors-professionals

14 associated master's degrees, including the University of Toulouse III–Paul Sabatier Master's in Cancerology run within the CRCT

24 vocational training courses plus 9 university and inter-university diplomas

95 medical-scientific events, including 53 organized by the IUCT-Oncopole



University training in step with the times

A multi-stage project initiated by Prof. O. Beyne-Rauzy and conducted in conjunction with all the disciplines involved in cancerology culminated in 2018 with the finalization of a complete teaching module for Master's students:

- The theoretical part of the module includes an e-learning component consisting of five specially designed SPOCs focusing on communicating bad news and the patient-doctor relationship (launched in 2018).
 - Students can personalize their choice of internships in order to focus on the cancer and hematology care pathways that interest them most (launched in 2015).
 - Training in medical decision-making teaches students how to resolve complex problems. Students, divided into five teams and advised by tutors, compete to see who can determine the most appropriate treatment pathways for complex pathologies (launched in 2015).
 - Use of mannequins to simulate invasive examinations such as pelvic examinations (launched in 2018).
 - Teaching of soft skills via sessions with simulated patients and debriefings with users (launched in 2018).
- Around 300 students completed this novel multimodal and multidisciplinary cancerology training module in 2018.

Postgraduate training for interns includes "student MDT meetings" to simulate the types of decision-making situations they will face in real MDT meetings, sessions on transversal themes in which students are divided into two teams and required to defend one of two opposing points of view on a controversial issue, and, since 2018, news-breaking workshops with simulated patients.



A 6th SPOC, focusing on the generalities of care pathways for cancer patients, presents many of the themes covered by the University of Paris Diderot's "Cancer diagnosis strategies" MOOC, and is complementary to it. Several nursing training institutes have integrated this MOOC into their programs since 2017.

A new inter-university diploma: "Breast cancer: from physiology to after cancer"

The Universities of Toulouse and Montpellier have joined forces to launch a new joint diploma designed by Prof. F. Trémollières and Prof. F. Dalenc. Taught by healthcare professionals from Toulouse, Montpellier and Nîmes, it consists of in-class courses, practical sessions and e-learning. The new course will begin at the IUCT-Oncopole in February 2019 with an initial group of around 15 students. This course adds to the eight other university and inter-university diplomas with which the IUCT-Oncopole is associated.

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.
- In addition, healthcare professionals and researchers are regularly invited to visit the IUCT-Oncopole's departments and facilities (pharmacy, radiotherapy department, etc.).
- Twenty-four vocational training courses are taught at the IUCT-Oncopole by the Institut Claudius Regaud's and GIPSE's training departments. Many programs incorporate modern training tools, such as SPOCs and the MYRE (MY Recordable E-learning) course, which was developed by Dr. L. Simon as a continuous self-training and evaluation tool for the radiotherapy technicians team.
- Finally, in order to allow healthcare professionals to adapt their training to their time constraints and to meet the demands of the younger generation, the IUCT-Oncopole is setting up its own e-learning platform. Called MyLittleTools, it will be available to interns in the spring of 2019 and opened up to other learners by 2020.

First Dosimetry School

The first edition of this new international training course for medical/research physicians was held at the IUCT-Oncopole on September 27 and 28, 2018. Steered by Dr. L. Vieillevine (ICR/IUCT-Oncopole Medical Physics and CRCT team 15), this intensive seminar on the dosimetry of small proton fields attracted fifteen participants (medical physicists) from France, Belgium and Lebanon. It was the first Dosimetry School to be held in France. Further Dosimetry Schools will be held in Spain, Great Britain and Belgium in 2019.

Information on therapeutic patient education

- The IUCT-Oncopole, in conjunction with patients' associations, holds numerous events 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. For example, on March 21, 2018, the IUCT-Oncopole, with support from the French Association for Cancer Care and Support (AFSOS), hosted the Supporter Tour, which highlights different aspects of supportive care and provides information to patients' and their families. In addition, the IUCT-Oncopole marked the French Palliative Care Association's (ASP) 30th birthday by organizing a week of events on the theme of caregivers.
- In August 2018, the Occitanie Regional Health Agency named the IUCT-Oncopole as the "sponsor and guarantor of the Cancerology Transversal Therapeutic Education Unit (UTEP, coordinator: E. Arfé) 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.
- In 2018, the Hematology Department's grafts unit began designing two TPE programs for patients who have received allogeneic grafts. Dr. A. Huynh is coordinating the project. The post-graft program (coordinator: F. Carantois) will provide support to patients during the post-allogeneic-graft monitoring phase, which often raises psychological, social and medical issues, and help improve post-graft quality of life. The project has been approved by the Occitanie Regional Health Agency and aims to include around 50 patients

in 2019. In addition, a pre-graft program (coordinator: L. Mercier) is being finalized. This program will help patients understand the long and sometimes difficult allogeneic graft process and, if possible, reduce the post traumatic stress many patients suffer following the pre-allogeneic graft information meeting, notably by enabling them to talk with people who have gone through the process. Regional Health Agency approval for this program will be sought in 2019.

BRCA Café Club

The BRCA Café Club is a new initiative that was launched under the auspices of the GENEPEY network in 2018 by J. Grondin (Oncogenetics CCO). Café Club meetings, held in a pleasant café in the center of Toulouse, give women with a hereditary predisposition to breast and ovarian cancer (carriers of a BRCA 1 or BRCA 2 genetic mutation) an opportunity to meet and discuss their situation.

TOW 2018

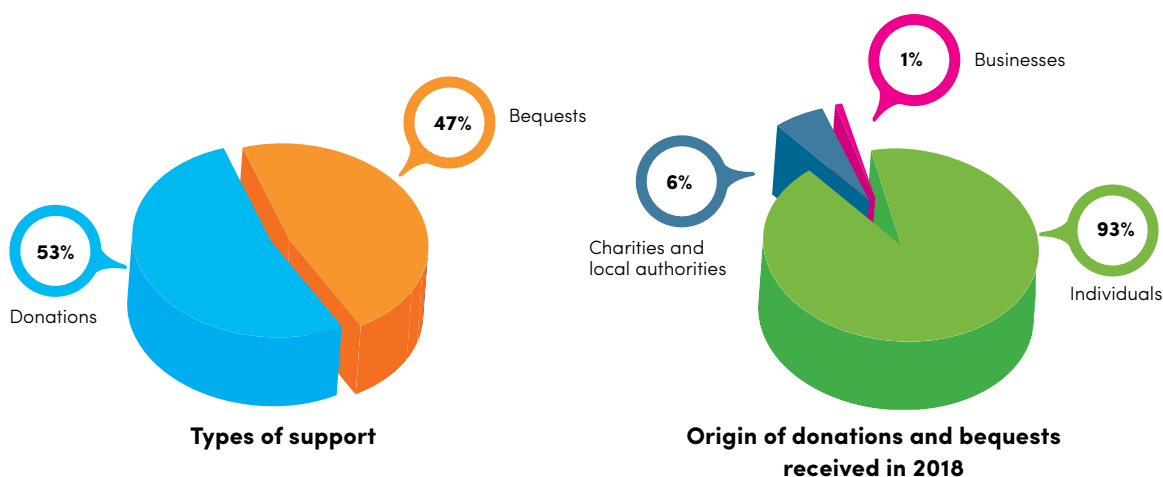
One of the biggest events of 2018 was Toulouse Onco Week – TOW 2018 – a bi-annual event that was launched in 2016 to mark World Cancer Day. It is organized by the IUCT GIP in conjunction with Toulouse University Hospital, the ICR, Inserm, the University of Toulouse III–Paul Sabatier, Toulouse Metropolitan Council, the Ligue Contre le Cancer, the Fondation Toulouse Cancer Santé, the Cancer–Bio–Santé innovation cluster and the Onco-Occitanie network.

TOW is a unique event in Europe, it provides a forum in which everyone involved in the fight against cancer – scientists, healthcare professionals, industry and charities – can discuss ways of more effectively combatting the disease. More than 2,000 people attended the week's events.



Support for our work

We would like to express our deepest gratitude to all those who supported us in 2018. Thanks to you – local authorities, businesses, charities, and, especially, private individuals – we are able to continue innovating and launching new projects to identify and develop new therapeutic strategies that will improve the quality of life of our patients and their families.



A total of 8,351 contributions were made to support our work, providing €1,035,586 in 2018.

59.39% (€615,077) of the donations and bequests received in 2018 were allocated directly to the IUCT-Oncopole’s research activities (covering 5.35% of operating costs).

In 2018, the Fondation Toulouse Cancer Santé received 2,366 donations, amounting to €502,690 (50% businesses, 50% individuals).

Main publications

List of papers in journals with an impact factor greater than 10:
(papers for which a member of the IUCT-Oncopole was the 1st, 2nd, penultimate or last author are highlighted in orange).

- Adam, J., Le Stang, N., **Rouquette, L.**, Cazes, A., Badoual, C., Pinot-Roussel, H., Tixier, L., Danel, C., Damiola, F., Dammotte, D., Penault-Llorca, F., Lantuéjoul, S., 2018b. **Multi-center harmonization study for PD-L1 IHC testing in non-small-cell lung cancer.** Ann. Oncol. 29, 953–958. <https://doi.org/10.1093/annonc/mdy014>
- Antonia, S.J., Villegas, A., Daniel, D., Vicente, D., Murakami, S., Hui, R., Kurata, T., Chiappori, A., Lee, K.H., de Wit, M., Cho, B.C., Bourhaba, M., Quantin, X., Tokito, T., Mekhail, T., Planchard, D., Kim, Y.-C., Karapetis, C.S., Hirret, S., Ostoros, G., Kubota, K., Gray, J.E., Paz-Ares, L., de Castro Carpeño, J., Faivre-Finn, C., Reck, M., Vansteenkiste, J., Spigel, D.R., Wadsworth, C., Melillo, G., Taboada, M., Dennis, P.A., Özgüroğlu, M., PACIFIC Investigators, [collab : **Mazières, J.**] 2018. **Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC.** N. Engl. J. Med. 379, 2342–2350. <https://doi.org/10.1056/NEJMoa1809697>
- Avet-Loiseau, H.**, 2018. **Introduction to the review series on advances in multiple myeloma.** Blood. <https://doi.org/10.1182/blood-2018-11-877795>
- Bailly, C., Carlier, T., Jamet, B., Eugene, T., Touzeau, C., **Attal, M.**, Hulin, C., Facon, T., Leleu, X., Perrot, A., Garderet, L., Macro, M., Caillot, D., Moreau, P., Kraeber-Bodere, F., Bodet-Milin, C., 2018. **Interim PET analysis in first line therapy of multiple myeloma: Prognostic value of ΔSUVmax in the FDG-avid patients of the IMAJEM study.** Clin. Cancer Res. <https://doi.org/10.1158/1078-0432.CCR-18-0741>
- Bolli, N., Biancon, G., Moarii, M., Gimondi, S., Li, Y., de Philippis, C., Maura, F., Sathiseelan, V., Tai, Y.-T., Mudie, L., O'Meara, S., Raine, K., Teague, J.W., Butler, A.P., Carniti, C., Gerstung, M., Bagratuni, T., Kastritis, E., Dimopoulos, M., Corradini, P., Anderson, K.C., Moreau, P., Minvielle, S., Campbell, P.J., Papaemmanuil, E., **Avet-Loiseau, H.**, Munshi, N.C., 2018. **Analysis of the genomic landscape of multiple myeloma highlights novel prognostic markers and disease subgroups.** Leukemia. <https://doi.org/10.1038/s41375-018-0037-9>
- Bolli, N., Maura, F., Minvielle, S., Gloznik, D., Szalaf, R., Fullam, A., Martincorena, I., Dawson, K.J., Samur, M.K., Zamora, J., Tarpey, P., Davies, H., Fulciniti, M., Shammas, M.A., Tai, Y.T., Magrangeas, F., Moreau, P., Corradini, P., Anderson, K., Alexandrov, L., Wedge, D.C., **Avet-Loiseau, H.**, Campbell, P., Munshi, N., 2018. **Genomic patterns of progression in smoldering multiple myeloma.** Nat Commun 9, 3363. <https://doi.org/10.1038/s41467-018-05058-y>
- Breda, A., Territo, A., Gausa, L., Tuğcu, V., Alcaraz, A., Musquera, M., Decaestecker, K., Desender, L., Stockle, M., Janssen, M., Fornara, P., Mohammed, N., Siena, G., Serni, S., Guirado, L., Facundo, C., **Doumerc, N.**, 2018. **Robot-assisted Kidney Transplantation: The European Experience.** Eur. Urol. 73, 273–281. <https://doi.org/10.1016/j.eururo.2017.08.028>
- Cleynen, A., Samur, M., Perrot, A., **Buisson, L.**, Maheo, S., Fulciniti, M., **Attal, M.**, Munshi, N., **Avet-Loiseau, H.**, **Corre, J.**, 2018. **Variable BCL2/BCL2L1 ratio in multiple myeloma with t(11;14).** Blood. <https://doi.org/10.1182/blood-2018-09-876433>
- 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, [collab : **Delord, J.-P.**] 2018. **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. [https://doi.org/10.1016/S0140-6736\(18\)31999-8](https://doi.org/10.1016/S0140-6736(18)31999-8)
- Conroy, T., Hammel, P., Hebbbar, M., Ben Abdelghani, M., Wei, A.C., Raoul, J.-L., Choné, L., Francois, E., Artru, P., Biagi, J.J., Lecomte, T., Assenat, E., Faroux, R., Ychou, M., Volet, J., Sauvanet, A., Breysacher, G., Di Fiore, F., Cripps, C., Kavan, P., Texereau, P., Bouhier-Leporrier, K., Khemis-ssa-Akouz, F., Legoux, J.-L., Juzyna, B., Gourgou, S., O'Callaghan, C.J., Jouffroy-Zeller, C., Rat, P., Malka, D., Castan, F., Bachet, J.-B., Canadian Cancer Trials Group and the Unicancer-GI-PRODIGE Group, [collab : **Guimbaud, R.**] 2018. **FOLFIRINOX or Gemcitabine as Adjuvant Therapy for Pancreatic Cancer.** N. Engl. J. Med. 379, 2395–2406. <https://doi.org/10.1056/NEJMoa1809775>
- Corre, J.**, Cleynen, A., **Robiou du Pont, S.**, **Buisson, L.**, Bolli, N., **Attal, M.**, Munshi, N., **Avet-Loiseau, H.**, 2018. **Multiple myeloma clonal evolution in homogeneously treated patients.** Leukemia. <https://doi.org/10.1038/s41375-018-0153-6>
- Costantini, A., Grynovska, M., Lucibello, F., Moisés, J., Pagès, F., Tsao, M.S., Shepherd, F.A., Bouchaab, H., Garassino, M., Aerts, J.G.J.V., **Mazières, J.**, Mondini, M., Berghmans, T., Meert, A.-P., Cadranet, J., 2018. **Immunotherapy: a new standard of care in thoracic malignancies? A summary of the European Respiratory Society research seminar of the Thoracic Oncology Assembly.** Eur. Respir. J. 51. <https://doi.org/10.1183/13993003.02072-2017>
- Cottu, P., D'Hondt, V., Dureau, S., Lerebours, F., Desmoulins, I., Heudel, P.-E., Duhoux, F.P., Levy, C., Mouret-Reynier, M.-A., **Dalenc, F.**, Frenel, J.-S., Jouannaud, C., Venat-Bouvet, L., Nguyen, S., Ferrero, J.-M., Canon, J.-L., Grenier, J., Callens, C., Gentien, D., Lemonnier, J., Vincent-Salomon, A., Delalogue, S., 2018. **Letrozole and palbociclib versus chemotherapy as neoadjuvant therapy of high-risk luminal breast cancer.** Ann. Oncol. <https://doi.org/10.1093/annonc/mdy448>
- Dejoie, T., **Corre, J.**, Caillon, H., Moreau, P., **Attal, M.**, **Loiseau, H.A.**, 2018. **Responses in multiple myeloma should be assigned according to serum, not urine, free light chain measurements.** Leukemia. <https://doi.org/10.1038/s41375-018-0339-y>

15. 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., Vargafig, J., Laghouati, S., Croisille, L., Voisin, A.-L., Godeau, B., Massard, C., Ribrag, V., Marabelle, A., Michel, M., Lambotte, O., 2018. **Haematological immune-related adverse events induced by anti-PD-1 or anti-PD-L1 immunotherapy: a descriptive observational study.** *Lancet Haematol.* [https://doi.org/10.1016/S2352-3026\(18\)30175-3](https://doi.org/10.1016/S2352-3026(18)30175-3)
16. Drilon, A., Lin, J.J., Filleron, T., Ni, A., Milia, J., Bergagnini, I., Hatzoglou, V., Velcheti, V., Offin, M., Li, B., Carbone, D.P., Besse, B., Mok, T., Awad, M.M., Wolf, J., Owen, D., Camidge, D.R., Riely, G.J., Peled, N., Kris, M.G., Mazieres, J., Gainor, J.F., Gautschi, O., 2018. **Brief Report: Frequency of Brain Metastases and Multikinase Inhibitor Outcomes in Patients with RET-Rearranged Lung Cancers.** *J Thorac Oncol.* <https://doi.org/10.1016/j.jtho.2018.07.004>
17. Duffaud, F., Mir, O., Boudou-Rouquette, P., Piperno-Neumann, S., Penel, N., Bompas, E., Delcambre, C., Kalbacher, E., Italiano, A., Collard, O., Chevreau, C., Saada, E., Isambert, N., Delaye, J., Schiffler, C., Bouvier, C., Vidal, V., Chabaud, S., Blay, J.-Y., French Sarcoma Group, 2018. **Efficacy and safety of regorafenib in adult patients with metastatic osteosarcoma: a non-comparative, randomised, double-blind, placebo-controlled, phase 2 study.** *Lancet Oncol.* [https://doi.org/10.1016/S1470-2045\(18\)30742-3](https://doi.org/10.1016/S1470-2045(18)30742-3)
18. Dumontet, C., Hulin, C., Dimopoulos, M.A., Belch, A., Dispenzieri, A., Ludwig, H., Rodon, P., Van Droogenbroeck, J., Qiu, L., Cavo, M., Van de Velde, A., Lahuerta, J.J., Allangba, O., Lee, J.H., Boyle, E., Perrot, A., Moreau, P., Manier, S., Attal, M., Roussel, M., Mohty, M., Mary, J.Y., Civet, A., Costa, B., Tinel, A., Gaston-Mathé, Y., Facon, T., 2018. **A predictive model for risk of early grade \geq 3 infection in patients with multiple myeloma not eligible for transplant: analysis of the FIRST trial.** *Leukemia.* <https://doi.org/10.1038/s41375-018-0133-x>
19. 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., 2018. **Long-term Clinical Outcomes and Biomarker Analyses of Atezolizumab Therapy for Patients With Metastatic Triple-Negative Breast Cancer: A Phase 1 Study.** *JAMA Oncol.* <https://doi.org/10.1001/jamaoncol.2018.4224>
20. Ettl, J., Quek, R.G.W., Lee, K.-H., Rugo, H.S., Hurvitz, S., Gonçalves, A., Fehrenbacher, L., Yerushalmi, R., Mina, L.A., Martin, M., Roché, H., Im, Y.-H., Markova, D., Bhattacharyya, H., Hannah, A.L., Eiermann, W., Blum, J.L., Litton, J.K., 2018. **Quality of life with talazoparib versus physician's choice of chemotherapy in patients with advanced breast cancer and germline BRCA1/2 mutation: patient-reported outcomes from the EMBRACA phase III trial.** *Ann. Oncol.* <https://doi.org/10.1093/annonc/mdy257>
21. Facon, T., Dimopoulos, M.A., Dispenzieri, A., Catalano, J.V., Belch, A., Cavo, M., Pinto, A., Weisel, K., Ludwig, H., Bahlis, N.J., Banos, A., Tiab, M., Delforge, M., Cavenagh, J.D., Galdes, C., Lee, J.-J., Chen, C., Oriol, A., De La Rubia, J., White, D., Binder, D., Lu, J., Anderson, K.C., Moreau, P., Attal, M., Perrot, A., Arnulf, B., Qiu, L., Roussel, M., Boyle, E., Manier, S., Mohty, M., Avet-Loiseau, H., Lelou, X., Ervin-Haynes, A., Chen, G., Houck, V., Benboubker, L., Hulin, C., 2018. **Final analysis of survival outcomes in the phase 3 FIRST trial of up-front treatment for multiple myeloma.** *Blood* 131, 301-310. <https://doi.org/10.1182/blood-2017-07-795047>
22. Ferrara, R., Mezquita, L., Texier, M., Lahmar, J., Audigier-Valette, C., Tessonier, L., Mazieres, J., Zalcman, G., Brosseau, S., Le Moulec, S., Leroy, L., Duchemann, B., Lefebvre, C., Veillon, R., Westeel, V., Koscielny, S., Champiat, S., Ferté, C., Planchard, D., Remon, J., Boucher, M.-E., Gazzah, A., Adam, J., Bria, E., Tortora, G., Soria, J.-C., Besse, B., Caramella, C., 2018. **Hyperprogressive Disease in Patients With Advanced Non-Small Cell Lung Cancer Treated With PD-1/PD-L1 Inhibitors or With Single-Agent Chemotherapy.** *JAMA Oncol.* <https://doi.org/10.1001/jamaoncol.2018.3676>
23. Ferrer, L., Gajj Levrá, M., Brevet, M., Antoine, M., Mazieres, J., Rossi, G., Chiari, R., Westeel, V., Poudenx, M., Letreut, J., Gervais, R., Osman, G., Girard, N., Toffart, A.C., Novello, S., Moro-Sibilot, D., 2018. **A brief report of transformation from Non-small cell to small cell lung cancer: Molecular and therapeutic characteristics.** *J Thorac Oncol.* <https://doi.org/10.1016/j.jtho.2018.08.2028>
24. Fonteyne, V., Ost, P., Bellmunt, J., Droz, J.P., Mongiat-Artus, P., Inman, B., Pailaud, E., Saad, F., Ploussard, G., 2018. **Curative Treatment for Muscle Invasive Bladder Cancer in Elderly Patients: A Systematic Review.** *Eur. Urol.* 73, 40-50. <https://doi.org/10.1016/j.eururo.2017.03.019>
25. Galateau Salle, F., Le Stang, N., Nicholson, A.G., Pissaloux, D., Churg, A., Klebe, S., Roggli, V., Tazelaar, H., Vignaud, J.M., Attanoos, R., Beasley, M.B., Begueret, H., Capron, F., Chirieac, L., Copin, M.C., Dacic, S., Danel, C., Foulet-Roge, A., Gibbs, A., Giusiano-Courcambeck, S., Hiroshima, K., Hofman, V., Husain, A., Kerr, K., Marchevsky, A., Nabeshima, K., Picquetot, J.M., Rouquette, L., Sagan, C., Sauter, J., Thivolet, F., Travis, W.D., Tsao, M.S., Weynand, B., Damiola, F., Scherpereel, A., Pignon, J.C., Lantuejoul, S., Rusch, V., Girard, N., 2018. **New insights on diagnostic reproducibility of biphasic mesotheliomas: a multi-institutional evaluation by the international mesothelioma panel from the MESOPATH reference center.** *J Thorac Oncol.* <https://doi.org/10.1016/j.jtho.2018.04.023>

26. Gandaglia, G., Ploussard, G., Valerio, M., Mattei, A., Fiori, C., Fossati, N., Stabile, A., Beauval, J.-B., Malavaud, B., Roumiguié, M., Robesti, D., Dell'Oglio, P., Moschini, M., Zamboni, S., Rakauskas, A., De Cobelli, F., Porpiglia, F., Montorsi, F., Briganti, A., 2018a. **A Novel Nomogram to Identify Candidates for Extended Pelvic Lymph Node Dissection Among Patients with Clinically Localized Prostate Cancer Diagnosed with Magnetic Resonance Imaging-targeted and Systematic Biopsies.** *Eur. Urol.* <https://doi.org/10.1016/j.eururo.2018.10.012>
27. Gandara, D.R., von Pawel, J., Mazieres, J., Sullivan, R., Helland, A., Han, J.-Y., Ponce Aix, S., Rittmeyer, A., Barlesi, F., Kubo, T., Park, K., Goldschmidt, J., Gandhi, M., Yun, C., Yu, W., Matheny, C., He, P., Sandler, A., Ballinger, M., Fehrenbacher, L., 2018. **Atezolizumab Treatment Beyond Progression in Advanced NSCLC: Results From the Randomized, Phase III OAK Study.** *J Thorac Oncol* 13, 1906–1918. <https://doi.org/10.1016/j.jtho.2018.08.2027>
28. Garassino, M.C., Cho, B.-C., Kim, J.-H., Mazières, J., Vansteenkiste, J., Lena, H., Corral Jaime, J., Gray, J.E., Powderly, J., Chouaid, C., Bidoli, P., Wheatley-Price, P., Park, K., Soo, R.A., Huang, Y., Wadsworth, C., Dennis, P.A., Rizvi, N.A., ATLANTIC Investigators, 2018. **Durvalumab as third-line or later treatment for advanced non-small-cell lung cancer (ATLANTIC): an open-label, single-arm, phase 2 study.** *Lancet Oncol.* 19, 521–536. [https://doi.org/10.1016/S1470-2045\(18\)30144-X](https://doi.org/10.1016/S1470-2045(18)30144-X)
29. Garderet, L., Kuhnowski, F., Berge, B., Roussel, M., Escoffre-Barbe, M., Lafon, I., Facon, T., Leleu, X., Karlin, L., Perrot, A., Moreau, P., Marit, G., Stoppa, A.-M., Royer, B., Chaleteix, C., Tiab, M., Araujo, C., Lenain, P., Macro, M., Voog, E., Benboubker, L., Allangba, O., Jourdan, E., Orcsini-Piocelle, F., Brechignac, S., Eveillard, J.-R., Belhadj, K., Wetterwald, M., Pegourie, B., Jaccard, A., Eisenmann, J.-C., Glaisner, S., Mohty, M., Hulin, C., Avet Loiseau, H., Mathiot, C., Attal, M., 2018. **Pomalidomide, cyclophosphamide, and dexamethasone for relapsed multiple myeloma.** *Blood.* <https://doi.org/10.1182/blood-2018-07-863829>
30. Gay, F., Jackson, G., Rosiñol, L., Holstein, S.A., Moreau, P., Spada, S., Davies, F., Lahuerta, J.J., Leleu, X., Bringhen, S., Evangelista, A., Hulin, C., Panzani, U., Cairns, D.A., Di Raimondo, F., Macro, M., Liberati, A.M., Pawlyn, C., Offidani, M., Spencer, A., Hájek, R., Terpos, E., Morgan, G.J., Bladé, J., Sonneveld, P., San-Miguel, J., McCarthy, P.L., Ludwig, H., Boccadoro, M., Mateos, M.-V., Attal, M., 2018. **Maintenance Treatment and Survival in Patients With Myeloma: A Systematic Review and Network Meta-analysis.** *JAMA Oncol.* <https://doi.org/10.1001/jamaoncol.2018.2961>
31. Gelderblom, H., Cropet, C., Chevreau, C., Boyle, R., Tattersall, M., Stacchiotti, S., Italiano, A., Piperno-Neumann, S., Le Cesne, A., Ferraresi, V., Penel, N., Duffaud, F., Cassier, P., Toulmonde, M., Casali, P., Taieb, S., Guillemaut, S., Metzger, S., Pérol, D., Blay, J.-Y., 2018. **Nilotinib in locally advanced pigmented villonodular synovitis: a multicentre, open-label, single-arm, phase 2 trial.** *Lancet Oncol.* [https://doi.org/10.1016/S1470-2045\(18\)30143-8](https://doi.org/10.1016/S1470-2045(18)30143-8)
32. Ghez, D., Calleja, A., Protin, C., Baron, M., Ledoux, M.-P., Damaj, G., Dupont, M., Dreyfus, B., Ferrant, E., Herbaux, C., Laribi, K., Le Calloch, R., Malphettes, M., Paul, F., Souchet, L., Truchan-Graczyk, M., Delavigne, K., Dartigeas, C., Ysebaert, L., 2018. **Early-onset invasive aspergillosis and other fungal infections in patients treated with ibru-tinib.** *Blood.* <https://doi.org/10.1182/blood-2017-11-818286>
33. 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., 2018. **Stromal protein ig-h3 reprogrammes tumour microenvironment in pancreatic cancer.** *Gut.* <https://doi.org/10.1136/gutjnl-2018-317570>
34. Guillerey, C., Harjunpää, H., Carrié, N., Kassem, S., Teo, T., Miles, K., Krumeich, S., Weulersse, M., Cuisinier, M., Stannard, K., Yu, Y., Minnie, S.A., Hill, G.R., Dougall, W.C., Avet-Loiseau, H., Teng, M.W.L., Nakamura, K., Martinet, L., Smyth, M.J., 2018. **TIGIT immune checkpoint blockade restores CD8+ T cell immunity against multiple myeloma.** *Blood.* <https://doi.org/10.1182/blood-2018-01-825265>
35. Günther, T., Tulipano, G., Dournaud, P., Bousquet, C., Csaba, Z., Kreienkamp, H.-J., Lupp, A., Korbonits, M., Castaño, J.P., Wester, H.-J., Culler, M., Melmed, S., Schulz, S., 2018. **International Union of Basic and Clinical Pharmacology. CV. Somatostatin Receptors: Structure, Function, Ligands, and New Nomenclature.** *Pharmacol. Rev.* 70, 763–835. <https://doi.org/10.1124/pr.117.015388>
36. Hansen, A.R., Massard, C., Ott, P.A., Haas, N.B., Lopez, J.S., Ejadi, S., Wallmark, J.M., Keam, B., Delord, J.-P., Aggarwal, R., Gould, M., Yang, P., Keefe, S.M., Piha-Paul, S.A., 2018. **Pembrolizumab for advanced prostate adenocarcinoma: findings of the KEYNOTE-028 study.** *Ann. Oncol.* 29, 1807–1813. <https://doi.org/10.1093/annonc/mdy232>
37. Hindíe, E., Récher, C., Zerdoud, S., Leenhardt, L., Avram, A.M., 2018. **Risk of Hematologic Malignancies After Radioactive Iodine Treatment of Thyroid Cancer: An Unjustified Warning.** *J. Clin. Oncol.* JCO2018781096. <https://doi.org/10.1200/JCO.2018.78.1096>
38. Hospital, M.-A., Jacquelin, A., Mazed, F., Saland, E., Lar-rue, C., Mondesir, J., Birsens, R., Green, A.S., Lambert, M., Sujobert, P., Gautier, E.-F., Salnot, V., Le Gall, M., Decroocq, J., Poulain, L., Jacque, N., Fontenay, M., Kosmider, O., Récher, C., Auberger, P., Mayeux, P., Bouscary, D., Sarry, J.-E., Tamburini, J., 2018. **RSK2 is a new Pim2 target with pro-survival functions in FLT3-ITD-positive acute myeloid leukemia.** *Leukemia* 32, 597–605. <https://doi.org/10.1038/leu.2017.284>
39. Hoyles, L., Fernández-Real, J.-M., Federici, M., Serino, M., Abbott, J., Charpentier, J., Heymes, C., Luque, J.L., Anthony, E., Barton, R.H., Chilloux, J., Myridakis, A., Martinez-Gili, L., Moreno-Navarrete, J.M., Benhamed, F.,

- Azalbert, V., Blasco-Baque, V., Puig, J., Xifra, G., Ricart, W., Tomlinson, C., Woodbridge, M., Cardellini, M., Davato, F., Cardolini, I., Porzio, O., Gentileschi, P., Lopez, E., Foulfelle, F., Butcher, S.A., Holmes, E., Nicholson, J.K., Postic, C., Burcelin, R., Dumas, M.-E., 2018a. **Molecular phenomics and metagenomics of hepatic steatosis in non-diabetic obese women.** *Nat. Med.* 24, 1070–1080. <https://doi.org/10.1038/s41591-018-0061-3>
40. Hoyles, L., Fernández-Real, J.-M., Federici, M., Serino, M., Abbott, J., Charpentier, J., Heymes, C., Luque, J.L., Anthony, E., Barton, R.H., Chilloux, J., Myridakis, A., Martínez-Gili, L., Moreno-Navarrete, J.M., Benhamed, F., Azalbert, V., Blasco-Baque, V., Puig, J., Xifra, G., Ricart, W., Tomlinson, C., Woodbridge, M., Cardellini, M., Davato, F., Cardolini, I., Porzio, O., Gentileschi, P., Lopez, E., Foulfelle, F., Butcher, S.A., Holmes, E., Nicholson, J.K., Postic, C., Burcelin, R., Dumas, M.-E., 2018b. **Publisher Correction: Molecular phenomics and metagenomics of hepatic steatosis in non-diabetic obese women.** *Nat. Med.* <https://doi.org/10.1038/s41591-018-0169-5>
41. Huquet, F., Chevret, S., Leguay, T., Thomas, X., Boissel, N., Escoffre-Barbe, M., Chevallier, P., Hunault, M., Vey, N., Bonmati, C., Lepretre, S., Marolleau, J.-P., Pabst, T., Rousselot, P., Buzyn, A., Cahn, J.-Y., Lhéritier, V., Béné, M.C., Asnafi, V., Delabesse, E., Macintyre, E., Chalandon, Y., Ifrah, N., Dombret, H., Group of Research on Adult ALL (GRAALL), 2018. **Intensified Therapy of Acute Lymphoblastic Leukemia in Adults: Report of the Randomized GRAALL-2005 Clinical Trial.** *J. Clin. Oncol.* JCO2017768192. <https://doi.org/10.1200/JCO.2017.76.8192>
42. Hulea, L., Gravel, S.-P., Morita, M., Cargnello, M., Uchenunu, O., Im, Y.K., Lehuédé, C., Ma, E.H., Leibovitch, M., McLaughlan, S., Blouin, M.-J., Parisotto, M., Papavasiliou, V., Lavoie, C., Larsson, O., Ohh, M., Ferreira, T., Greenwood, C., Bridon, G., Avizonis, D., Ferbeyre, G., Siegel, P., Jones, R.G., Muller, W., Ursini-Siegel, J., St-Pierre, J., Pollak, M., Topisirovic, I., 2018. **Translational and HIF-1-Dependent Metabolic Reprogramming Underpin Metabolic Plasticity and Responses to Kinase Inhibitors and Biguanides.** *Cell Metab.* 28, 817–832.e8. <https://doi.org/10.1016/j.cmet.2018.09.001>
43. Komrokji, R., Garcia-Manero, G., Ades, L., Prebet, T., Steensma, D.P., Jurcic, J.G., Sekeres, M.A., Berdeja, J., Savona, M.R., Beyne-Rauzy, O., Stamatoullas, A., DeZern, A.E., Delaunay, J., Borthakur, G., Rifkin, R., Boyd, T.E., Laadem, A., Vo, B., Zhang, J., Puccio-Pick, M., Attie, K.M., Fenaux, P., List, A.F., 2018. **Sotatercept with long-term extension for the treatment of anaemia in patients with lower-risk myelodysplastic syndromes: a phase 2, dose-ranging trial.** *Lancet Haematol.* [https://doi.org/10.1016/S2352-3026\(18\)30002-4](https://doi.org/10.1016/S2352-3026(18)30002-4)
44. Lavaud, P., Gravis, G., Foulon, S., Joly, F., Oudard, S., Priou, F., Latorzeff, I., Mourey, L., Soulié, M., Delva, R., Krakowskij, I., Laquerre, B., Théodore, C., Ferrero, J.M., Beuzeboc, P., Habibian, M., Rolland, F., Deplanque, G., Pouessel, D., Zanetta, S., Berdah, J.F., Dauba, J., Baciuchka, M., Platini, C., Linassier, C., Tubiana-Mathieu, N., Machiels, J.P., Kouri, C.E., Ravaud, A., Suc, E., Eymard, J.C., Hasbini, A., Bousquet, G., Culine, S., Boher, J.-M., Tergemina-Clain, G., Legoupil, C., Fizazi, K., 2018. **Anticancer Activity and Tolerance of Treatments Received Beyond Progression in Men Treated Upfront with Androgen Deprivation Therapy With or Without Docetaxel for Metastatic Castration-naïve Prostate Cancer in the GETUG-AFU 15 Phase 3 Trial.** *Eur. Urol.* 73, 696–703. <https://doi.org/10.1016/j.eururo.2017.09.022>
45. Le Guellec, S., Lesluyes, T., Sarot, E., Valle, C., Filleron, T., Rochaix, P., Valentin, T., Pérot, G., Coindre, J.-M., Chibon, F., 2018. **Validation of the Complexity Index in SARCOMAS prognostic signature on formalin-fixed, paraffin-embedded, soft tissue sarcomas.** *Ann. Oncol.* <https://doi.org/10.1093/annonc/mdy194>
46. Lewin, J., Soria, J.-C., Stathis, A., Delord, J.-P., Peters, S., Awada, A., Aftimos, P.G., Bekradda, M., Rezaei, K., Zeng, Z., Hussain, A., Perez, S., Siu, L.L., Massard, C., 2018. **Phase Ib Trial With Birabresib, a Small-Molecule Inhibitor of Bromodomain and Extraterminal Proteins, in Patients With Selected Advanced Solid Tumors.** *J. Clin. Oncol.* JCO2018782292. <https://doi.org/10.1200/JCO.2018.78.2292>
47. Litton, J.K., Rugo, H.S., Ettl, J., Hurvitz, S.A., Gonçalves, A., Lee, K.-H., Fehrenbacher, L., Yerushalmi, R., Mina, L.A., Martin, M., Roché, H., Im, Y.-H., Quek, R.G.W., Markova, D., Tudor, I.C., Hannah, A.L., Eiermann, W., Blum, J.L., 2018. **Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation.** *N. Engl. J. Med.* 379, 753–763. <https://doi.org/10.1056/NEJMoa1802905>
48. Longué, M., Cabarrou, B., Wallet, J., Brodowicz, T., Roché, H., Boher, J.M., Delord, J.P., Penel, N., Filleron, T., 2018. **The importance of jointly analyzing treatment administration and toxicity associated with targeted therapies: a case study of regorafenib in soft tissue sarcoma patients.** *Ann. Oncol.* <https://doi.org/10.1093/annonc/mdy168>
49. Loubière, S., Drezet, A., Beau-Faller, M., Moro-Sibilot, D., Friard, S., Wislez, M., Blons, H., Daniel, C., Westeel, V., Madroszyk, A., Léna, H., Merle, P., Mazières, J., Zalcman, G., Lacave, R., Antoine, M., Morin, F., Missy, P., Barlesi, F., Auquier, P., Cadranet, J., French Cooperative Thoracic Intergroup (IFCT), 2018. **Cost-effectiveness of KRAS, EGFR and ALK testing for decision making in advanced nonsmall cell lung carcinoma: the French IFCT-PREDICT.amm study.** *Eur. Respir. J.* 51. <https://doi.org/10.1183/13993003.01467-2017>
50. Ludwig, H., Delforge, M., Facon, T., Einsele, H., Gay, F., Moreau, P., Avet-Loiseau, H., Boccadoro, M., Hajek, R., Mohy, M., Cavo, M., Dimopoulos, M.A., San-Miguel, J.F., Terpos, E., Zweegman, S., Garderet, L., Mateos, M.-V., Cook, G., Leleu, X., Goldschmidt, H., Jackson, G., Kaiser, M., Weisel, K., van de Donk, N.W.C.J., Waage, A., Beksac, M., Mellqvist, U.H., Engelhardt, M., Caers, J., Driessen, C., Bladé, J., Sonneveld, P., 2018. **Prevention and manage-**

- ment of adverse events of novel agents in multiple myeloma: a consensus of the European Myeloma Network. *Leukemia*.
51. Maio, M., Lewis, K., Demidov, L., Mandalà, M., Bondarenko, I., Ascierto, P.A., Herbert, C., Mackiewicz, A., Rutkowski, P., Guminski, A., Goodman, G.R., Simmons, B., Ye, C., Yan, Y., Schadendorf, D., BRIM8 Investigators [colab : Meyer, N.], 2018. **Adjuvant vemurafenib in resected, BRAFV600mutation-positive melanoma (BRIM8): a randomised, double-blind, placebo-controlled, multicentre, phase 3 trial.** *Lancet Oncol.* 19, 510–520. [https://doi.org/10.1016/S1470-2045\(18\)30106-2](https://doi.org/10.1016/S1470-2045(18)30106-2)
 52. 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., 2018. **The role of irradiated heart and left ventricular volumes in heart failure occurrence after childhood cancer.** *Eur. J. Heart Fail.* <https://doi.org/10.1002/ejhf.1376>
 53. Marisa, L., Svrcek, M., Collura, A., Becht, E., Cervera, P., Wanherdrick, K., Buhard, O., Goloudina, A., Jonchère, V., Selves, J., Milano, G., Guenot, D., Cohen, R., Colas, C., Laurent-Puig, P., Olschwang, S., Lefèvre, J.H., Parc, Y., Boige, V., Lepage, C., André, T., Fléjou, J.-F., Dérangère, V., Ghiringhelli, F., de Reynies, A., Duval, A., 2018. **The Balance Between Cytotoxic T-cell Lymphocytes and Immune Checkpoint Expression in the Prognosis of Colon Tumors.** *J. Natl. Cancer Inst.* 110. <https://doi.org/10.1093/jnci/djx136>
 54. Maura, F., Petljak, M., Lionetti, M., Cifola, I., Liang, W., Pinatel, E., Alexandrov, L.B., Fullam, A., Martincorena, I., Dawson, K.J., Angelopoulos, N., Samur, M.K., Szalat, R., Zamora, J., Tarpey, P., Davies, H., Corradini, P., Anderson, K.C., Minvielle, S., Neri, A., Avet-Loiseau, H., Keats, J., Campbell, P.J., Munshi, N.C., Bolli, N., 2018. **Biological and prognostic impact of APOBEC-induced mutations in the spectrum of plasma cell dyscrasias and multiple myeloma cell lines.** *Leukemia* 32, 1044–1048. <https://doi.org/10.1038/leu.2017.345>
 55. Méjean, A., Ravaud, A., Thezenas, S., Colas, S., Beauval, J.-B., Bensalah, K., Geoffrois, L., Thiery-Vuillemin, A., Cormier, L., Lang, H., Guy, L., Gravis, G., Rolland, F., Linossier, C., Lechevallier, E., Beisland, C., Aitchison, M., Oudard, S., Patard, J.-J., Theodore, C., Chevreau, C., Laguerre, B., Hubert, J., Gross-Goupil, M., Bernhard, J.-C., Albiges, L., Timsit, M.-O., Leuret, T., Escudier, B., 2018. **Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma.** *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1803675>
 56. Merveilleux du Vignaux, C., Dansin, E., Mhanna, L., Greillier, L., Pichon, E., Kerjouan, M., Clement-Duchene, C., Menecier, B., Westeel, V., Robert, M., Quantin, X., Zalcman, G., Thiberville, L., Lena, H., Molina, T., Calcaño, F., Fournel, P., Mazieres, J., Besse, B., Girard, N., 2018. **Systemic therapy in advanced thymic epithelial tumors: Insights from the RYTHMIC prospective cohort.** *J Thorac Oncol.* <https://doi.org/10.1016/j.jtho.2018.08.005>
 57. Meyer, C., Burmeister, T., Gröger, D., Tsaar, G., Fehina, L., Renneville, A., Sutton, R., Venn, N.C., Emerenciano, M., Pombo-de-Oliveira, M.S., Barbieri Blunck, C., Almeida Lopes, B., Zuna, J., Trka, J., Ballerini, P., Lapillonne, H., De Braekeleer, M., Cazzaniga, G., Corral Abascal, L., van der Velden, V.H.J., Delabesse, E., Park, T.S., Oh, S.H., Silva, M.L.M., Lund-Aho, T., Juvonen, V., Moore, A.S., Heidenreich, O., Vormoor, J., Zerkalenkova, E., Olshanskaya, Y., Bueno, C., Menendez, P., Teigler-Schlegel, A., Zur Stadt, U., Lentes, J., Göhring, G., Kustanovich, A., Aleinikova, O., Schäfer, B.W., Kubetzko, S., Madsen, H.O., Gruhn, B., Duarte, X., Gameiro, P., Lippert, E., Bidef, A., Cayuela, J.M., Clappier, E., Alonso, C.N., Zwaan, C.M., van den Heuvel-Eibrink, M.M., Izraeli, S., Trakhtenbrot, L., Archer, P., Hancock, J., Möricke, A., Alten, J., Schrappe, M., Stannulla, M., Strehl, S., Attarbaschi, A., Dworzak, M., Haas, O.A., Panzer-Grümayer, R., Sedék, L., Szczepański, T., Caye, A., Suarez, L., Cavé, H., Marschalek, R., 2018. **The MLL recombinome of acute leukemias in 2017.** *Leukemia* 32, 273–284. <https://doi.org/10.1038/leu.2017.213>
 58. Mezquita, L., Auclin, E., Ferrara, R., Charrier, M., Remon, J., Planchard, D., Ponce, S., Ares, L.P., Leroy, L., Audigier-Valette, C., Felip, E., Zerón-Medina, J., Garrido, P., Broseau, S., Zalcman, G., Mazieres, J., Caramela, C., Lahmar, J., Adam, J., Chaput, N., Soria, J.C., Besse, B., 2018. **Association of the Lung Immune Prognostic Index With Immune Checkpoint Inhibitor Outcomes in Patients With Advanced Non-Small Cell Lung Cancer.** *JAMA Oncol.* <https://doi.org/10.1001/jamaoncol.2017.4771>
 59. Mignard, X., Ruppert, A.-M., Antoine, M., Vasseur, J., Girard, N., Mazieres, J., Moro-Sibilo, D., Fallet, V., Rabbe, N., Thivolet-Bejui, F., Rouquette, I., Lantuejoul, S., Cortot, A., Saffroy, R., Cadranet, J., Lemoine, A., Wislez, M., 2018. **Brief report: c-MET overexpression as a poor predictor of MET amplifications or exon 14 mutations in lung sarcomatoid carcinomas.** *J Thorac Oncol.* <https://doi.org/10.1016/j.jtho.2018.08.008>
 60. Morschhauser, F., Fowler, N.H., Feugier, P., Bouabdallah, R., Tilly, H., Palomba, M.L., Fruchart, C., Libby, E.N., Casasnovas, R.-O., Flinn, I.W., Haioun, C., Maisonneuve, H., Ysebaert, L., Bartlett, N.L., Bouabdallah, K., Brice, P., Ribrag, V., Daguindau, N., Le Gouill, S., Pica, G.M., Martin Garcia-Sancho, A., López-Guillermo, A., Larouche, J.-F., Ando, K., Gomes da Silva, M., André, M., Zachée, P., Sehn, L.H., Tobinai, K., Cartron, G., Liu, D., Wang, J., Xerri, L., Salles, G.A., RELEVANCE Trial Investigators, 2018. **Rituximab plus Lenalidomide in Advanced Untreated Follicular Lymphoma.** *N. Engl. J. Med.* 379, 934–947. <https://doi.org/10.1056/NEJMoa1805104>
 61. Musto, P., Anderson, K.C., Attal, M., Richardson, P.G., Badros, A., Hou, J., Comenzo, R., Du, J., Durie, B.G.M., San Miguel, J., Einsele, H., Chen, W.M., Garderet, L., Pietran-tono, G., Hillengass, J., Kyle, R.A., Moreau, P., Lahuerta,

- J.J., Landgren, O., Ludwig, H., Larocca, A., Mahindra, A., Cavo, M., Mazumder, A., McCarthy, P.L., Nouel, A., Rajkumar, S.V., Reiman, A., Riva, E., Sezer, O., Terpos, E., Tureson, I., Usmani, S., Weiss, B.M., Palumbo, A., **International Myeloma Working Group, 2018. Second primary malignancies in multiple myeloma: an overview and IMWG consensus.** *Ann. Oncol.* 29, 1074. <https://doi.org/10.1093/annonc/mdx160>
62. Nagarajan, N., Dupret-Bories, A., Karabulut, E., Zorlutuna, P., Vrana, N.E., 2018. **Enabling personalized implant and controllable biosystem development through 3D printing.** *Biotechnol. Adv.* <https://doi.org/10.1016/j.biotechadv.2018.02.004>
63. Nakamura, K., Kassem, S., Cleynen, A., Chrétien, M.-L., Guilleroy, C., Putz, E.M., Bald, T., Förster, I., Vuckovic, S., Hill, G.R., Masters, S.L., Chesi, M., Bergsagel, P.L., Avet-Loiseau, H., Martinet, L., Smyth, M.J., 2018. **Dysregulated IL-18 Is a Key Driver of Immunosuppression and a Possible Therapeutic Target in the Multiple Myeloma Microenvironment.** *Cancer Cell.* <https://doi.org/10.1016/j.ccell.2018.02.007>
64. Novello, S., Mazières, J., Oh, I.-J., de Castro, J., Migliorino, M.R., Helland, Å., Dziadziuszko, R., Griesinger, F., Kotb, A., Zeaiter, A., Cardona, A., Balas, B., Johannsdottir, H.K., Das-Gupta, A., Wolf, J., 2018. **Alectinib versus chemotherapy in crizotinib-pretreated anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer: results from the phase III ALUR study.** *Ann. Oncol.* <https://doi.org/10.1093/annonc/mdy121>
65. Pal, S.K., Rosenberg, J.E., Hoffman-Censits, J.H., Berger, R., Quinn, D.I., Galsky, M.D., Wolf, J., Dittrich, C., Keam, B., Delord, J.-P., Schellens, J.H.M., Gravis, G., Medioni, J., Maroto, P., Sriuranpong, V., Charoentum, C., Burris, H.A., Grünwald, V., Petrylak, D., Vaishampayan, U., Gez, E., De Giorgi, U., Lee, J.-L., Voortman, J., Gupta, S., Mortazavi, A., Vaughn, D.J., Isaacs, R.E., Parker, K., Chen, X., Yu, K., Porter, D., Sharma, S., Graus Porta, D., Bajorin, D.F., 2018. **Efficacy of BGJ398, a fibroblast growth factor receptor 1-3 inhibitor, in patients with previously treated advanced urothelial carcinoma with FGFR3 alterations.** *Cancer Discov.* <https://doi.org/10.1158/2159-8290.CD-18-0229>
66. 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., 2018. **PAX5 P80R mutation identifies a novel subtype of B-cell precursor acute lymphoblastic leukemia with favorable outcome.** *Blood.* <https://doi.org/10.1182/blood-2018-10-882142>
67. Paz-Ares, L., Luft, A., Vicente, D., Tafreshi, A., Gümüş, M., Mazières, J., Hermes, B., Çay Şenler, F., Csösz, T., Fülöp, A., Rodríguez-Cid, J., Wilson, J., Sugawara, S., Kato, T., Lee, K.H., Cheng, Y., Novello, S., Halmos, B., Li, X., Lubiniecki, G.M., Piperdi, B., Kowalski, D.M., KEYNOTE-407 Investigators, 2018. **Pembrolizumab plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer.** *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa1810865>
68. Perrot, A., Lauwers-Cances, V., Corre, J., Robillard, N., Hulin, C., Chretien, M.-L., Dejoie, T., Maheo, S., Stoppa, A.-M., Pegourie, B., Karlin, L., Garderet, L., Arnulf, B., Doyen, C., Meuleman, N., Royer, B., Eveillard, J.-R., Benboubker, L., Dib, M., Decaux, O., Jaccard, A., Belhadj, K., Brechignac, S., Kolb, B., Fohrer, C., Mohty, M., Macro, M., Richardson, P.G., Carlton, V., Moorhead, M., Willis, T., Faham, M., Anderson, K.C., Harousseau, J.-L., Leleu, X., Facon, T., Moreau, P., Attal, M., Avet-Loiseau, H., Munshi, N., 2018b. **Minimal residual disease negativity using deep sequencing is a major prognostic factor in multiple myeloma.** *Blood.* <https://doi.org/10.1182/blood-2018-06-858613>
69. Pigneux, A., Béné, M.C., Salmi, L.-R., Dumas, P.-Y., Delaunay, J., Bonmati, C., Guièze, R., Luquet, I., Cornillet-Lefebvre, P., Delabesse, E., Ianotto, J.-C., Ojeda-Urbe, M., Hunault, M., Banos, A., Fornecker, L.M., Bernard, M., Jourdan, E., Vey, N., Zerazhi, H., Hishri, Y., Mineur, A., Asselineau, J., Delepine, R., Cahn, J.-Y., Ifrah, N., Récher, C., French Innovative Leukemia Organization, 2018. **Improved Survival by Adding Lomustine to Conventional Chemotherapy for Elderly Patients With AML Without Unfavorable Cytogenetics: Results of the LAM-SA 2007 FILO Trial.** *J. Clin. Oncol.* JCO2018787366. <https://doi.org/10.1200/JCO.2018.78.7366>
70. Ploussard, G., 2018a. **Re: Salvage High-intensity Focused Ultrasound (HIFU) for Locally Recurrent Prostate Cancer After Failed Radiation Therapy: Multi-institutional Analysis of 418 Patients.** *Eur. Urol.* 73, 140–141. <https://doi.org/10.1016/j.eururo.2017.09.031>
71. Ploussard, G., Gandaglia, G., Borgmann, H., de Visschere, P., Heidegger, I., Kretschmer, A., Mathieu, R., Surcel, C., Tilki, D., Tsaor, I., Valerio, M., van den Bergh, R., Ost, P., Briganti, A., EAU-YAU Prostate Cancer Working Group, 2018b. **Salvage Lymph Node Dissection for Nodal Recurrent Prostate Cancer: A Systematic Review.** *Eur. Urol.* <https://doi.org/10.1016/j.eururo.2018.10.041>
72. Renneville, A., Attias, P., Thomas, X., Bally, C., Hayette, S., Farhat, H., Eclache, V., Marceau-Renaut, A., Cassinat, B., Feuillard, J., Terré, C., Delabesse, E., Park, S., Lejeune, J., Chevret, S., Adès, L., Preudhomme, C., Fenaux, P., 2018. **Genetic analysis of therapy-related myeloid neoplasms occurring after intensive treatment for acute promyelocytic leukemia.** *Leukemia.* <https://doi.org/10.1038/s41375-018-0137-6>
73. Rouvière, O., Puech, P., Renard-Penna, R., Claudon, M., Roy, C., Mège-Lechevallier, F., Decaussin-Petrucci, M., Dubreuil-Chambardel, M., Magaud, L., Remontet, L., Ruffion, A., Colombel, M., Crouzet, S., Schott, A.-M., Lemaître, L., Rabilloud, M., Grenier, N., MRI-FIRST Investigators [collab : Malavaud, B., Portalez, D.], 2018. **Use of prostate systematic and targeted biopsy on the basis**

- of multiparametric MRI in biopsy-naïve patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study.** *Lancet Oncol.* [https://doi.org/10.1016/S1470-2045\(18\)30569-2](https://doi.org/10.1016/S1470-2045(18)30569-2)
74. Rozman, J., Rathkolb, B., Oestereich, M.A., Schütt, C., Ravindranath, A.C., Leuchtenberger, S., Sharma, S., Kistler, M., Willershäuser, M., Brommage, R., Meehan, T.F., Mason, J., Haselimeshadi, H., IMPC Consortium, Hough, T., Mallon, A.-M., Wells, S., Santos, L., Lelliott, C.J., White, J.K., Sorg, T., Champy, M.-F., Bower, L.R., Reynolds, C.L., Flenniken, A.M., Murray, S.A., Nutter, L.M.J., Svenson, K.L., West, D., Tocchini-Valentini, G.P., Beaudet, A.L., Bosch, F., Braun, R.B., Dobbie, M.S., Gao, X., Heralut, Y., Moshiri, A., Moore, B.A., Kent Lloyd, K.C., Mckerlie, C., Masuya, H., Tanaka, N., Flicek, P., Parkinson, H.E., Sedlacek, R., Seong, J.K., Wang, C.-K.L., Moore, M., Brown, S.D., Tschöp, M.H., Wurst, W., Klingenspor, M., Wolf, E., Beckers, J., Machicao, F., Peter, A., Staiger, H., Häring, H.-U., Grallert, H., Campillos, M., Maier, H., Fuchs, H., Gailus-Durner, V., Werner, T., Hrabe de Angelis, M. [collab : Huynh, A.]. 2018. **Identification of genetic elements in metabolism by high-throughput mouse phenotyping.** *Nat Commun* 9, 288. <https://doi.org/10.1038/s41467-017-01995-2>
75. Rugo, H.S., Roche, H., Thomas, E., Chung, H.C., Lerzo, G.L., Vasyutin, I., Patel, A., Vahdat, L., 2018b. **Efficacy and Safety of Ixabepilone and Capecitabine in Patients With Advanced Triple-negative Breast Cancer: a Pooled Analysis From Two Large Phase III, Randomized Clinical Trials.** *Clin. Breast Cancer.* <https://doi.org/10.1016/j.clbc.2018.07.024>
76. Ruhstaller, T., Giobbie-Hurder, A., Colleoni, M., Jensen, M.-B., Ejlersten, B., de Azambuja, E., Neven, P., Lång, 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, 2018. **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.* JCO1800440. <https://doi.org/10.1200/JCO.18.00440>
77. Samur, M.K., Minvielle, S., Gulla, A., Fulciniti, M., Cleynen, A., Aktas Samur, A., Szalat, R., Shamma, M., Magranga, F., Tai, Y.-T., Auclair, D., Keats, J., Richardson, P., Attal, M., Moreau, P., Anderson, K.C., Parmigiani, G., Avet-Loiseau, H., Munshi, N.C., 2018. **Long intergenic non-coding RNAs have an independent impact on survival in multiple myeloma.** *Leukemia.* <https://doi.org/10.1038/s41375-018-0116-y>
78. Saussele, S., Richter, J., Guilhot, J., Gruber, F.X., Hjorth-Hansen, H., Almeida, A., Janssen, J.J.W.M., Mayer, J., Koskenvesa, P., Panayiotidis, P., Olsson-Strömberg, U., Martinez-Lopez, J., Rousselot, P., Vestergaard, H., Ehren-crona, H., Kairisto, V., Machová Poláková, K., Müller, M.C., Mustjoki, S., Berger, M.G., Fabarius, A., Hofmann, W.-K., Hochhaus, A., Pfirrmann, M., Mahon, F.-X., EURO-SKI investigators [collab : Huguet, F.], 2018. **Discontinuation of tyrosine kinase inhibitor therapy in chronic myeloid leukaemia (EURO-SKI): a prespecified interim analysis of a prospective, multicentre, non-randomised, trial.** *Lancet Oncol.* 19, 747–757. [https://doi.org/10.1016/S1470-2045\(18\)30192-X](https://doi.org/10.1016/S1470-2045(18)30192-X)
79. Schlumberger, M., Leboulloux, S., Catargi, B., Deandreis, D., Zerdoud, S., Bardet, S., Rusu, D., Godbert, Y., Buffet, C., Schwartz, C., Vera, P., Morel, O., Benisvy, D., Bournaud, C., Toubert, M.-E., Kelly, A., Benhamou, E., Borget, I., 2018. **Outcome after ablation in patients with low-risk thyroid cancer (ESTIMABL1): 5-year follow-up results of a randomised, phase 3, equivalence trial.** *Lancet Diabetes Endocrinol.* [https://doi.org/10.1016/S2213-8587\(18\)30113-X](https://doi.org/10.1016/S2213-8587(18)30113-X)
80. Siu, L.L., Even, C., Mesia, R., Remenar, E., Daste, A., De-lord, 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., 2018. **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.* <https://doi.org/10.1001/jamaoncol.2018.4628>
81. Socinski, M.A., Jotte, R.M., Cappuzzo, F., Orlandi, F., Stroyakovskiy, D., Nogami, N., Rodríguez-Abreu, D., Moro-Sibilot, D., Thomas, C.A., Barlesi, F., Finley, G., Kelsch, C., Lee, A., Coleman, S., Deng, Y., Shen, Y., Kowanzet, M., Lopez-Chavez, A., Sandler, A., Reck, M., IMpower150 Study Group [collab : Mazières, J.], 2018. **Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC.** *N. Engl. J. Med.* 378, 2288–2301. <https://doi.org/10.1056/NEJMoa1716948>
82. Szalat, R., Samur, M.K., Fulciniti, M., Lopez, M., Nanjappa, P., Cleynen, A., Wen, K., Kumar, S., Perini, T., Calkins, A.S., Reznichenko, E., Chauhan, D., Tai, Y.-T., Shamma, M.A., Anderson, K.C., Ferman, J.-P., Arnulf, B., Avet-Loiseau, H., Lazaro, J.-B., Munshi, N.C., 2018. **Nucleotide excision repair is a potential therapeutic target in multiple myeloma.** *Leukemia* 32, 111–119. <https://doi.org/10.1038/leu.2017.182>
83. Tordo, J., O'Leary, C., Antunes, A.S.L.M., Palomar, N., Aldrin-Kirk, P., Basche, M., Bennett, A., D'Souza, Z., Gleitz, H., Godwin, A., Holley, R.J., Parker, H., Liao, A.Y., Rouse, P., Youshani, A.S., Dridi, L., Martins, C., Levade, T., Stacey, K.B., Davis, D.M., Dyer, A., Clément, N., Björklund, T., Ali, R.R., Agbandje-McKenna, M., Rahim, A.A., Pshezhetsky, A., Waddington, S.N., Linden, R.M., Bigger, B.W., Hencckaerts, E., 2018. **A novel adeno-associated virus capsid with enhanced neurotropism corrects a lysosomal transmembrane enzyme deficiency.** *Brain.* <https://doi.org/10.1093/brain/awy126>

84. Toren, P., Hoffman, A., Ding, K., Joncas, F.-H., Turcotte, V., Caron, P., Pouliot, F., Fradet, Y., Lévesque, É., Guillemette, C., Klotz, L., 2018. **Serum Sex Steroids as Prognostic Biomarkers in Patients Receiving Androgen Deprivation Therapy for Recurrent Prostate Cancer: A Post Hoc Analysis of the PR.7 Trial.** *Clin. Cancer Res.* 24, 5305–5312. <https://doi.org/10.1158/1078-0432.CCR-18-1187>
85. Toulmonde, M., Penel, N., Adam, J., Chevreau, C., Blay, J.-Y., Le Cesne, A., Bompas, E., Piperno-Neumann, S., Cousin, S., Grellety, T., Ryckewaert, T., Bessede, A., Ghiringhelli, F., Pulido, M., Italiano, A., 2018. **Use of PD-1 Targeting, Macrophage Infiltration, and IDO Pathway Activation in Sarcomas: A Phase 2 Clinical Trial.** *JAMA Oncol* 4, 93–97. <https://doi.org/10.1001/jamaoncol.2017.1617>
86. 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., Tauziède-Espariat, A., Delisle, M.-B., Figarella-Branger, D., Bourdeaut, F., Rigau, V., 2018. **ETMR-like infantile cerebellar embryonal tumors in the extended morphologic spectrum of DICER1-related tumors.** *Acta Neuropathol.* <https://doi.org/10.1007/s00401-018-1935-7>
87. Valentin, T., Lesluyes, T., Le Guellec, S., Chibon, F., 2018. **Chemotherapy in localized Soft Tissue Sarcoma: will we soon have to treat grade 1 tumours? Update on CINSARC performances.** *Ann. Oncol.* <https://doi.org/10.1093/annonc/mdy465>
88. Walker, B.A., Mavrommatis, K., Wardell, C.P., Ashby, T.C., Bauer, M., Davies, F., Rosenthal, A., Wang, H., Qu, P., Hoering, A., Samur, M., Towfic, F., Ortiz, M., Flynt, E., Yu, Z., Yang, Z., Rozelle, D., Obenauer, J., Trotter, M., Auclair, D., Keats, J., Bolli, N., Fulciniti, M., Szalat, R., Moreau, P., Durie, B., Stewart, A.K., Goldschmidt, H., Raab, M.S., Einsele, H., Sonneveld, P., San Miguel, J., Lonial, S., Jackson, G.H., Anderson, K.C., Avet-Loiseau, H., Munshi, N., Thakurta, A., Morgan, G., 2018a. **A high-risk, Double-Hit, group of newly diagnosed myeloma identified by genomic analysis.** *Leukemia.* <https://doi.org/10.1038/s41375-018-0196-8>
89. Walker, B.A., Mavrommatis, K., Wardell, C.P., Ashby, T.C., Bauer, M., Davies, F.E., Rosenthal, A., Wang, H., Qu, P., Hoering, A., Samur, M., Towfic, F., Ortiz, M., Flynt, E., Yu, Z., Yang, Z., Rozelle, D., Obenauer, J., Trotter, M., Auclair, D., Keats, J., Bolli, N., Fulciniti, M., Szalat, R., Moreau, P., Durie, B., Stewart, A.K., Goldschmidt, H., Raab, M.S., Einsele, H., Sonneveld, P., San Miguel, J., Lonial, S., Jackson, G.H., Anderson, K.C., Avet-Loiseau, H., Munshi, N., Thakurta, A., Morgan, G., 2018b. **Identification of novel mutational drivers reveals oncogene dependencies in multiple myeloma.** *Blood.* <https://doi.org/10.1182/blood-2018-03-840132>
90. Wendum, D., Layese, R., Ganne-Carrié, N., Bourcier, V., Merabtene, F., Cagnot, C., Sauce, E., Bedossa, P., Terris, B., Selves, J., Bioulac-Sage, P., Sturm, N., Sattoune, C., Nahon, P., Roudot-Thoraval, F., Ziol, M., ANRS CO12 CirVir group, 2018. **Influence of progenitor-derived regeneration markers on HCV-related cirrhosis outcome (ANRS CO12 CirVir cohort).** *Hepatology.* <https://doi.org/10.1002/hep.29927>
91. Wu, X., Kabalane, H., Kahli, M., Petryk, N., Laperrousaz, B., Jaszczyszyn, Y., Drillon, G., Nicolini, F.-E., Perot, G., Robert, A., Fund, C., Chibon, F., Xia, R., Wiels, J., Argoul, F., Maguer-Satta, V., Arneodo, A., Audit, B., Hyrien, O., 2018. **Developmental and cancer-associated plasticity of DNA replication preferentially targets GC-poor, lowly expressed and late-replicating regions.** *Nucleic Acids Res.* <https://doi.org/10.1093/nar/gky849>



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