INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
Oncopole

ACTIVITY REPORT
2021

COLLECTIVE EXPERTISE TO FIGHT CANCER

FOCUS RESEARCH

CONTENTS

DETAILS PER TEAM

Toulouse Cancer Research Center (CRCT)

CRCT T2i team

Anti-tumor immunity and immunotherapy

Coordinator: Pr Maha Ayyoub

Specific themes
Tumor Antigen-Specific T Cells | T Cell Depletion | Immune Checkpoint Inhibitor Immunotherapy | Clinical Trials | Genomics | Transcriptomics | Preclinical Orthotopic Models | Cancer Vaccines

PROJETS

· **Role of tumor antigen-specific T cells in clinical responses to immunotherapies** – Coordinators: Dr Carlos Gomez Roca and Dr Anna Salvioni – More info

· **Setting up clinical trials and immune monitoring of patients treated with immunotherapy** – Coordinator: Dr Clara-Maria Scarlata – More info

· **Targeting autophagy in cancer immunotherapy** – Coordinator: Dr Sylvie Giuriato – More info

· **Impact of tumor immune microenvironments on the response to immunotherapies** – Coordinator: Dr Christel Devaud – More info

· **Immune complexity of epithelial cancers** – Coordinator: Pr Alejandra Martínez – More info

FOCUS 2021

The T2i team is participating in two clinical trials to evaluate TG4050, the personalized anti-cancer vaccine developed by Transgene. These trials were launched in 2021 and will focus on gynecological and ENT cancers. The first patient with non-viral-induced ENT cancer to benefit from this vaccine in Europe is a patient from the IUCT-Oncopole. The T2i team collaborates with the immunomonitoring team to ensure the follow-up of these two innovative phase 1 clinical trials conducted at the IUCT-Oncopole. More about this project

→ Discover the team's publications

CRCT MICROPANC team

Microenvironment and therapeutic resistance in pancreatic neoplasms

Coordinator: Pr Maha Ayyoub

Specific themes
Pancreatic Cancer | Microenvironment & Cancer-associated Fibroblasts | Metastasis | Translational Regulation | Metabolic Reprogramming | Matrix Rigidity & Mechano-transduction | Patient-Derived Experimental Models | Targeted Nanotherapies | (Polysome) RNAseq & Bioinformatics | Matrisome | Multiplexed Tissue Imaging

PROJETS

· **Identification of tumor-stroma crosstalk involved in the aggressiveness of pancreatic cancer** – Coordinator: Dr Corinne Bousquet – More info

· **Targeted nanotherapies to treat pancreatic adenocarcinoma** – Coordinator: Dr Véronique Gigoux – More info

· **Role of fibroblastic Focal-Adhesion Kinase (FAK) in pancreatic adenocarcinoma** – Coordinator: Dr Christine Jean – More info

· **Translational analysis of mRNAs as a new approach to classify pancreatic tumors** – Coordinator: Dr Yvan Martineau – More info

FOCUS 2021

Research coordinated by Dr Rémi Samain and Dr Corinne Bousquet has demonstrated that the development of metastases in pancreatic cancer could be blocked by normalizing the secretion of proteins produced by fibroblasts present in the microenvironment. The team is exploring the combination of a somatostatin analogue (SOM230) and the chemotherapy gemcitabine as a new therapeutic strategy that is particularly promising for limiting the development of metastases. Read the article

Discover the team's publications

CRCT RADOPT team

Optimizing radiation therapy: from molecular signaling pathways to clinical trials

Coordinator: Pr Elizabeth Moyal

Specific themes
Radiotherapy | Tumor Treating Fields (TTF) | Stem Cells | Plasticity | Translational Research | Resistance | Heterogeneity | Metabolism | Treatment | Mathematics and Physics | Image Modeling | Artificial Intelligence

PROJETS

· **Role of metabolism in radiation-induced plasticity and heterogeneity of glioma stem cells** – Coordinator: Dr Anthony Lemarié – More info

· **Optimizing the determination of absorbed dose in external radiotherapy** – Coordinator: Dr Laure Vieillevigne – More info

· **Resistance of glioblastoma stem cells to Tumor Treating Fields** – Coordinator: Dr Valérie Gouaze-Andersson – More info

· **Optimization of radiotherapy target volumes and evaluation of treatment response with multi-modal imaging** – Coordinator: Dr Soléakhéna Ken – More info

· **Invasiveness of glioblastoma stem cells: analysis of mechanisms involved** – Coordinator: Dr Catherine Seva- More info

· **Dose calculation in radiotherapy by Monte-Carlo method** – Coordinator: Dr Luc Simon- More info

· **Radiation-induced transdifferentiation of glioblastoma stem cells into endothelial-like cells** – Coordinators: Pr Monique Courtade-Saïdi & Dr Solène Evrard – More info

· **Optimization of radiotherapy: inverse problems and AI for quality assurance, treatment planning and dosimetry** – Coordinator: Dr Xavier Franceries – More info

· **Effect of macroautophagy inhibition on glioblastoma stem cells** – Coordinator: Dr Laurent Baricault – More info

FOCUS 2021

GAMMORA: a tool developed at the CRCT to generate Monte-Carlo GATE simulations
GAMMORA is a project developed at the CRCT under the leadership of Dr Luc Simon. The objective is to generate Monte-Carlo GATE simulations easily for radiotherapy for the VARIAN TrueBeam accelerator, one of the most common in the world. The tool is available in open source under LGPL license. Learn more about it

→ Discover the team's publications

CRCT IGAALD team

Impact of genetic alterations on the development of acute leukemia

Coordinator: Pr Eric Delabesse

Specific themes
Clinical Research | Myelodysplastic Syndromes | Acute Type B Myeloid Leukemia | National Registry | GATA2 transcription Factor

PROJETS

· **Leukemic development of hemophilia with GATA2 germline alterations** – Coordinator: Dr Pr Marlène Pasquet – More info

· **Characterization and targeting of pre-leukemic stem cells in acute type B lymphoblastic leukemia** – Coordinator: Dr Bastien Gerby – More info

· **Functions of CHK1 kinase and USP7 deubiquitinylase in normal and leukemic hematopoiesis**– Coordinator: Dr Christine Didier – More info

· **Genomic analysis of acute leukemia** – Coordinator: Pr Eric Delabesse – More info

· **Study of germline alterations of transcription factors in acute leukemia** – Coordinator: Pr Dr Cyril Broccardo – More info

FOCUS 2021

Germline alterations of transcription factors in acute leukemia
In collaboration with the University Hospital of Lille, the team coordinated by Cyril Broccardo, identified the PAX5R38H mutation in a family in which all three children developed acute type B lymphoblastic leukemia (B-ALL). PAX5 is a central factor in the production of functional B cells and is often somatically altered in B-ALL. The team showed that the PAX5R38H mutant loses PAX functionality, thus blocking B cells at very early stages, but reacquires properties that may explain the initiation of leukemia. This transformation requires an alteration of the Ras and Jak/Stat pathways. Read the article

→ Discover the team's publications

CRCT DynAct team

Molecular dynamics of lymphocyte interactions

Coordinator: Dr Salvatore Valitutti

This team is part of the Labex TOUCAN.

Specific themes
Immunological synapse | Cytotoxic T lymphocytes | Tumor immunology | Real-time imaging techniques | Tumor immune evasion | Pyroptosis | Computational biology | In silico modeling | Computer vision | Cartesian genetic programming | CD8+ resident memory T cells | Tumor microenvironment

PROJETS

· **The struggle between cytotoxic T lymphocytes and tumor cells at the lytic synapse** – Coordinator: Dr Salvatore Valitutti – More info

· **Modeling and computer vision applied to the study of competitive CTL/target cell interactions** – Coordinators: Dr Salvatore Valitutti & Dr Sylvain Cussat-Blanc – More info

· **Functions and regulation of tissue memory-resident CD8+ T cells** – Coordinator: Dr Fanny Lafouresse – More info

· **Study of target cell pyroptosis in the context of CTL-induced death** – Coordinator: Dr Brienne McKenzie – More info

FOCUS 2021

Launch of the ATTACK project (ERC Grant)
In November 2020, Salvatore Valitutti was named co-recipient of the prestigious European ERC Synergy Grant, together with three other partners: Jens Retting (Saarland University, Hamburg, Germany), Cosima Baldari (University of Siena, Italy) and Michael Dustin (University of Oxford, UK). The total amount of the funded project «ATTACK – Analysis of the tactical arsenal of T cells to kill cancer cells» is 10 million euros over 6 years. The ATTACK consortium is based on a major discovery made by the IUCT-Oncopole and Oxford University teams: a complementary attack mechanism launched by CTL cells based on supramolecular attack particles (SMAPs) that are rapidly released and are capable of killing target cells, which can be both pathogen-infected cells and cancer cells. This will potentially lead to new therapeutic approaches to be developed at the IUCT-Oncopole. More about this project

Discover the team's publications

CRCT SIGNATHER team

Cellular signaling, oncogenesis and therapeutics

Coordinators: Pr Gilles Favre and Dr Olivier Sordet

Specific themes
Oncogenic signaling | RTK/RAS/MAPK | RHOGTPases | Lung cancer | Translational research | Liquid biopsies | Biomarkers | Clinical trials | Targeted therapies | Resistance | Biotechnology | Split GFP | DNA breaks | Genomic instability | Transcription

PROJETS

· **Transcriptional DNA breaks and human diseases** – Coordinator: Dr Olivier Sordet – More info

· **Early detection of cancer and treatment resistance** – Coordinators: Dr Anne Pradines & Pr Julien Mazières – More info

· **Rho GTPase-mediated cellular plasticity in bronchial cancer progression and therapy resistance** – Coordinator: Dr Olivier Calvayrac – More info

· **Molecular mechanisms and modulation of small GTPase activity in cancer** – Coordinator: Dr Stéphanie Cabantous – More info

FOCUS 2021

Development of a technique to monitor RHO activation in tumors
In collaboration with the IUCT-Oncopole Molecular Biology Laboratory and the company CISBIO Bioassays, the SIGNATHER team has developed a new ELISA technique to measure the levels of active RHO proteins in cell lines and tumor samples at the nanomolar level. The technique is inexpensive and easily reproducible in the laboratory, without the need for special equipment. The team observed an increase in RHOA and RHOC protein activation in tumor samples compared to healthy tissues, as well as differences between the levels of active RHO proteins and their expression levels in tumor samples, thus allowing them to be classified into different subcategories. More about this study

Discover the team's publications

CRCT R'n Blood team

RNA biology in hematological tumors

Coordinators: Dr Stéphane Pyronnet & Dr Fabienne Meggetto

This team is part of the Labex TOUCAN.

Specific themes
Translation of mRNA| Non-coding RNA | miRNAs | lncRNAs | CircRNAs | Reticulum stress | Acute leukemia | Pediatric T-cell lymphoma | Oncogenesis | Treatment resistance | Targeted therapies | Biomarkers

PROJETS

· **Translational control of gene expression in hematological tumors** – Coordinator: Dr Stéphane Pyronnet – More info

· **Regulation of microRNAs and circular RNAs and their theranostic potential in ALK-associated anaplastic large cell T lymphoma** – Coordinators: Dr Fabienne Meggetto & Dr Laurence Lamant – More info

· **Role of endoplasmic reticulum stress in the progression and resistance of acute myeloid leukemia** – Coordinator: Dr Christian Touriol – More info

· **Involvement of long non-coding RNAs in chemoresistance of acute myeloid leukemia** – Coordinator: Dr Marina Bousquet– More info

FOCUS 2021

Circular RNAs in hematological malignancies
In 2018, Erika Brunet and Loélia Babin were the first to identify circular RNAs derived from the chromosomal translocation of the gene coding for the oncogenic protein NPM-ALK. At the end of 2021, the R'n Blood team published a state-of-the-art review in JCI Insight that focused on circular RNAs in blood cancers and their potential as biomarkers of treatment resistance. Read more

Discover the team's publications

CRCT INOV team

Cholesterol metabolism and therapeutic innovations

Coordinators: Dr Marc Poirot & Dr Sandrine Silvente-Poirot

Specific themes
Oncometabolism | Cholesterol | Oxysterol | Oncosterone | Secretory vesicles | Exosomes | Dendrogenin | Nuclear receptors | Enzymes | Metabolic imaging

PROJETS

· **Identification and characterization of new sterol metabolites** – Coordinator: Dr Marc Poirot – More info

· **Biochemical and pharmacological control of oncosterone production** – Coordinators: Dr Philippe De Medina – More info

· **Study of signaling pathways activated by oncosterone and dendrogenin A** – Coordinator: Dr Sandrine Silvente-Poirot – More info

· **New probes for non-invasive tumor detection by medical imaging** – Coordinator: Dr Philippe de Medina & Pr Frédéric Courbon – More info

· **Study of cholesterol metabolism deregulation in neuroendocrine cancers** – Coordinator: Dr Lavinia Vija – More info

FOCUS 2021

Deregulation of cholesterol metabolism in breast and thyroid cancer
The team, which has been accredited by the Ligue Contre le Cancer, is working on the deregulation of cholesterol metabolism in certain cancers. The team characterized the appearance of a tumor promoter called oncosterone and the disappearance of a tumor suppressor metabolite called dendrogenin A in cancer settings. Both molecules are derived from a common precursor that is derived from cholesterol. The quest is therefore to characterize this new metabolic pathway and its deregulation in cancers, especially in breast cancer. The team has established strategies for the identification and design of regulators of this pathway. The objective is to develop new therapeutic strategies for the detection and chemoprevention of cancers. These projects are made possible thanks to funding from academic and charitable sources, and thanks to the generosity of associations.

Discover the team's publications

CRCT SigDYN team

Integrated cellular signaling and PI3K isoforms

Coordinator: Dr Julie Guillermet-Guibert

Specific themes
Oncogenic Signaling | PI3K | Targeted Therapies | Resistance | Tumor Niche | Cancer Initiation | Mechanobiology | Compression | Genetically Engineered Mice | Tumor Imaging | Pancreatic Cancer | Ovarian Cancer

PROJETS

· **Better diagnosis and treatment with targeted therapies** – Coordinator: Dr Céline Basset – More info

· **Importance of PI3K isoforms as a major factor in mechanotransduction** – Coordinators: Dr Morgan Delarue and Dr Mickael Di-Luoffo – More info

· **Importance of PI3K isoforms in pathophysiology** – Coordinators: Dr Benoît Thibault and Dr. Marlène Dufresne – More info

FOCUS 2021

CLUSTER – Understanding tumor progression

Morphological aspects reflect genetic changes. Can they be used to better diagnose tumor progression?
The objective of this project is to develop and automate the analysis of morphological parameters of effusions such as the presence of clusters of carcinoma cells. By identifying morphological characteristics, it will be possible on the one hand to improve the diagnosis and to specify the prognosis, and on the other hand to discover the molecular mechanisms which underpin them in order to create new targeted therapies. CLUSTER, coordinated by Dr. Céline Basset and Dr. Julie Guillermet-Guibert, received €100,000 in funding from the TranIsational@IUCT-O call for projects in 2021.

Discover the team's publications

CRCT NetB(IO)² team

Network Biology and PI3K isoforms

Coordinator: Dr Vera Pancaldi

Specific themes
Computational biology | Network theory | Spatial and single cell transcriptomics | Genome architecture | Mathematical models | Immune system | Heterogeneity and tumor microenvironment | Epigenomics

PROJETS

· **Deconvolution (description of the composition of the tumor microenvironment): towards personalized medicine** – Coordinator: Dr Leila Khajavi – More info

· **Modeling and simulation of cellular interactions in the tumor by individual-centered approaches** – Coordinator: Dr Nina Verstraete – More info

· **Boolean regulatory networks of cellular phenotypes** – Coordinator: Dr Malvina Marku – More info

· **Study of the spatial organization of the tumor microenvironment and multiomics approaches** – Coordinator: Dr Vera Pancaldi – More info

· **Epigenomics and chromatin networks** – Coordinator: Dr Benoit Aliaga– More info

Chair in Bioinformatics in Oncology

The Toulouse Cancer Health Foundation, Inserm and the Pierre Fabre Research Institute, which are major stakeholders on the Toulouse Oncopole campus, have joined forces to create the first chair in bioinformatics in oncology for a period of 5 years. Vera Pancaldi, a physicist with expertise in systems biology, has been appointed to head it since its creation in 2018 at the CRCT.

FOCUS 2021

Development of the Tysserand software

Entitled Tysserand, the Python library developed by the NetB(IO)² team allows the extraction of networks from tissue images and other types of spatial data (proteomic or transcriptomic). These networks can then be used to study the spatial distribution patterns of cells that exhibit specific phenotypes in the tissue of each patient. The first important application was in the now completed pilot phase of the LungPredict project, which aims to better characterize lung cancer patients based on the composition and spatial patterns of cells in and around the tumor.
A grant from the Cancéropôle Grand Sud-Ouest was also obtained in 2021 to produce and analyze spatial transcriptomics data. The first papers have been published on dynamic simulations of intercellular interactions in cancer. See the article presenting the tool

→ Discover the team's publications

CRCT MELASPHINX team

Ceramide metabolism in melanoma: from molecular mechanisms to immunotherapy

Coordinators: Pr Bruno Ségui & Dr Nathalie Andrieu

Specific themes
Melanoma | Metabolism | Ceramide | Immunotherapy | TNF

PROJETS

· **Role of ceramide metabolism in epidermal homeostasis and melanoma progression** – Coordinator: Dr Nathalie Andrieu – More info

· **Interconnections between TNF signaling and ceramide metabolism in melanoma** – Coordinator: Pr Bruno Ségui – More info

· **Reprogramming ceramide metabolism to overcome resistance to immunotherapies** – Coordinator: Dr Céline Colacios – More info

· **Metabolites and enzymes of ceramide metabolism as biomarkers of resistance to immunotherapies** – Coordinator: Pr Nicolas Meyer – More info

· **TNF: a new target in immunotherapy?** – Coordinator: Pr Nicolas Meyer – More info

FOCUS 2021

A new immunotherapy strategy for melanoma

The team showed that neutralization of TNFα, a major inflammatory cytokine, potentiates the response to anti-PD-1 in murine models of melanoma. This work underpins the scientific rationale for the TICIMEL clinical trial (NTC03293784), which aims to evaluate the safety, tolerability and anti-tumor activity of anti-TNFα molecules (certolizumab or infliximab) in combination with ipilimumab and nivolumab in patients with advanced melanoma. Initial results are promising, with signs of activation and maturation of the immune response, fewer side effects in patients treated with infliximab, and to date a better clinical response rate in the certolizumab-treated cohort. Investigations are ongoing in an expansion cohort.

→ Discover the team's publications

CRCT NoLymIT team

New immunotherapies for lymphoma

Coordinator: Pr Camille Laurent

This team is part of the Labex TOUCAN.

Specific themes
B lymphoma/LLC | Microenvironment & Cytotoxic T-cells | Mechanism of immune escape & post-transcriptional regulation of immune checkpoints | Biomarkers of response/progression | 3D models | Therapeutic screening | Single-cell RNAseq | Bioinformatics

PROJETS

· **Single-cell mapping of the anti-tumor immune response in lymphoma: phenotypic and functional study of lymphocytes infiltrating lymph node lymphomas** – Coordinator: Pr Camille Laurent – More info

· **Tumor microenvironment screening: tumor-associated macrophage blockade and Tγδ lymphocyte activation** – Coordinator: Dr Mary Poupot – More Info

· **Characterization and therapeutic targeting of a novel immunoregulatory mechanism** – Coordinator: Dr Don Marc Franchini – More info

· **Resistance of leukemic and immune cells to targeted therapies in chronic lymphocytic leukemia** – Coordinator: Dr Anne Quillet-Mary – More info

· **PDLS: a central player for identifying new therapeutic targets in NHL** – Coordinator: Dr Christine Bezombes – More info

FOCUS 2021

CALYM-JANSSEN grant

A partnership was signed between Astra Zeneca, Inserm Transfert and the Carnot Institute CALYM network in 2020 to develop preclinical and translational projects for a duration of three years, with funding for up to two projects per year. A new CALYM-Janssen grant was launched in 2021. The CATALY project led by Dr Christine Bezombes and Prof Camille Laurent is one of the two winners. This project aims to evaluate the potential of CD39 as a new therapeutic target, and to provide clinicians with a solid rationale to extend the study to larger phase 1 cohorts integrating CD39 inhibitors in the treatment of follicular lymphoma and diffuse large B-cell lymphoma, in combination with GA101 and/or nivolumab. Read more

Discover the team's publications

CRCT GENIM team

Oncogenomics and immunology of myeloma

Coordinators: Dr Ludovic Martinet & Pr Hervé Avet-Loiseau

This team is part of the Labex TOUCAN.

Specific themes
Multiple Myeloma | Genomic Changes | Clonal Selection | Resistance | Immunity | Cytotoxic Lymphocyte | Immune Escape | Immunotherapy

PROJETS

· **Molecular alterations and heterogeneity in myeloma cells** – Coordinators: Pr Hervé Avet-Loiseau & Dr Jill Corre – More info

· **Cytotoxic cell landscape controlling myeloma development and clinical outcome** – Coordinator: Dr Ludovic Martinet – More info

· **Mechanism underlying tumor-associated cytotoxic T cell dysfunction** – Coordinator: Dr Ludovic Martinet – More info

· **Finding new immunotherapeutic strategies for myeloma** – Coordinator: Ludovic Martinet – More info

FOCUS 2021

ARC Foundation's Team of Honor Award

Prof. Hervé Avet-Loiseau received the award for his work in identifying molecular biomarkers that can be used to anticipate the risk of myeloma recurrence in patients, even with the most recent treatments. Their work has also shed light on several mechanisms that cause these hematological cancers to escape immune system surveillance. These discoveries now make it possible to envisage the development of new immunotherapy strategies.
In January 2021, part of this work was published in the prestigious journal Immunity. A new immunotherapy target was found that could optimize strategies already widely used (anti PD-1/PD-L1/CTLA-4) or others under development. Read more

→ Discover the team's publications

CRCT METAML team

Metabolism and therapeutic resistance in acute myeloid leukemia

Coordinator: Dr Jean-Emmanuel Sarry

This team is part of the Labex TOUCAN.

Specific themes
Acute myeloid leukemias | Metabolism | Therapeutic resistance | Oxidative stress | Metabolic adaptation | Transcriptional and post-transcriptional regulation | Autophagy | Leukemic microenvironment | Signaling | Tumor heterogeneity

PROJETS

· **Role of metabolic dialogue and systemic metabolism in mitochondrial adaptation and therapeutic resistance of AML cells** – Coordinators: Dr Jean-Emmanuel Sarry & Dr Fanny Grannat – More info

· **Transcriptional and post-transcriptional regulators of metabolism and response to AML therapy** – Coordinator: Dr Margherita Ghisi – More info

· **Leukemic and host autophagy, a major player in the therapeutic resistance of AML cells** – Coordinators: Dr Carine Joffre & Dr Laura Poillet – More info

FOCUS 2021

In 2021, Dr Laura Poillet-Perez was the recipient of the L'Oréal For Women in Science Foundation Young Talent Award. Her research involves understanding the involvement of autophagy in therapeutic resistance in leukemia. The role of this mechanism in cancer is complex since autophagy can both contribute to and prevent tumor growth and resistance to therapy. While this makes autophagy a promising therapeutic target, the exact mechanisms involved remain elusive. The results of his research will make it possible to design new treatments and avoid the risk of relapse, a major therapeutic challenge for this blood cancer with a high mortality rate. More info.

Discover the team's publications

CRCT RNAreg team

RNA binding proteins and genotoxic stress

Coordinator: Dr Stefania Millevoi

Specific themes
Head and Neck Cancers (HNSCC) | DNA Damage Response | Molecular Mechanisms of Therapeutic Resistance | Autophagy | Post-transcriptional Regulation | Epitranscriptome | mRNA Translation | RNA Binding Proteins | G-quadruplex RNA Structures | Omics Approaches | Bioinformatics

PROJETS

· **G-quadruplex structures & cellular adaptation to stress** – Coordinator: Dr Anne Cammas – More info

· **DNA damage response regulators in post-transcriptional control** – Coordinator: Dr Stéphane Manenti – More info

· **Link between RNA & autophagy** – Coordinator: Dr Estelle Espinos – More info

· **RNA binding proteins, autophagy & response to therapies in HNSCC** – Coordinators: Dr Stefania Millevoi & Pr Sébastien Vergez – More info

FOCUS 2021

In 2021, INSERM created the RNAreg team, which had been emerging at the CRCT since 2016. It includes experts in protein synthesis (Stefania Millevoi and Anne Cammas) and autophagy (Estelle Espinos, Stéphane Manenti), as well as clinicians (Sébastien Vergez) who investigate the biology of RNA in HNSCC cancer in response to genotoxic stress. Work published in 2021 focused on the functional duality of autophagy in cancer cells and its role in resistance (read the article) and metabolic stress (collaborative work with Arnaud Besson (CBI, Toulouse) – read the article), as well as the involvement of non-canonical RNA structures (collaboration with Erik Dassi (CIBIO, Trento, Italy) – read the article) in the mitochondrial protein synthesis involved in resistance to treatments (collaboration with Eleonora Leucci, (Ku, Leuven, Belgium) – read the article)

→ Discover the team's publications

CRCT ImPact team

Therapeutic innovation in pancreatic cancer

Coordinator: Dr Pierre Cordelier

Specific themes
Pancreatic Cancer | Oncogenesis | Resistance | Innovative Therapies | Regulation of Gene Expression | Protein-Protein Interaction | Intracellular Antibodies | Oncolytic Viruses | Gene Therapy | Immunotherapy | Interdisciplinarity

PROJETS

· **Role of genome remodeling and replication in gene expression and therapeutic resistance** – Coordinator: Dr Jérôme Torrisani – More info

· **Oncoproteins and protein-protein interactions involved in therapeutic resistance** – Coordinator: Dr Nicolas Bery – More info

· **Mechanisms of infection by oncolytic viruses and new approaches to immunotherapy** – Coordinators: Pr Louis Buscail & Dr Pierre Cordelier – More info

FOCUS 2021

In collaboration with the LAAS-CNRS, the CRCT ImPact team demonstrated the potential of the µLAS microfluidic system for detecting and quantifying the microRNA called miR-21 in less than a minute. The team already demonstrated that miR-21 can serve as a biomarker in pancreatic cancer. These results were obtained without amplification, and the detection limit measured was 2pM. Regarding the LAAS, its researchers are now working on improving the sensitivity of the technology, especially for the detection and quantification of new circulating biomarkers of clinical interest identified by the CRCT team. More info

Oncolytic viruses are promising new therapies that infect, replicate specifically in tumor cells and induce their death by different pathways, while remobilizing an antitumor immune response. In collaboration with the National Veterinary School in Toulousve and the company NeoVirTech, the ImPACT team has produced the first oncolytic virus equipped with NeoVirTech's ANCHOR technology. The team has shown that it is possible to monitor in real time the replication, and thus the efficacy, of the myxoma-derived SG33 virus in primary pancreatic cancer cells, both in vitro and in vivo. This heralds numerous perspectives, including precision virotherapy, for the management of cancer patients. See the article

→ Discover the team's publications

CRCT DIAD team

Personalization of cancer drug doses

Coordinator: Pr Etienne Chatelut

Specific themes
Pharmacokinetics | Pharmacogenetics | Treatment personalization | Pharmacological therapy monitoring | Liquid chromatography | Theranostic radiolabeled molecules | Family genetic predisposition

PROJETS

· **MATADOR and EXPECT projects: Identification of new predictive factors of male breast cancer (MATADOR) and young colon cancer (EXPECT)** – Coordinator: Dr Christine Toulas – More info

· **Oral therapies: PK/PD relationships and impact of metabolites in compliance detection** – Coordinators: Dr Félicien Le Louedec & Dr Florent Puisset – More info

· **Pharmacokinetic modeling of radiolabeled antibodies to understand resistance mechanisms in immunotherapy** – Coordinator: Dr. Melanie White-Koning – More info

· **Quantifying the sources of inter-individual variability in hormone therapy exposure** – Coordinator: Dr Fabienne Thomas – More info

· **Pharmacokinetics and theranostic radiolabeled molecules** – Coordinator: Dr Lawrence Dierickx – More info

· **Pharmacokinetics and innovative therapeutics** – Coordinator: Dr Ben Allal – More info

FOCUS 2021

Optimization of ibritunib monitoring

The team is particularly interested in the TDM (Therapeutic Drug Monitoring) of ibrutinib, whose limited accumulation in plasma does not allow classic follow-up by measuring the residual concentration alone. CT analyses of this molecule are based on the study of the area under the concentration-time curve (AUCIBRU). Work carried out by the team in collaboration with the IUCT-Oncopole pharmacy led to the identification of a limited sampling strategy (LSS) to estimate the AUCIBRU value associated with the Bayesian statistic. According to their results, three samples taken before and up to 4 hours after the dose administration make it possible to reliably estimate the exposure to ibrutinib. More info

→ Discover the team's publications

CRCT ONCOSARC team

Oncogenesis of sarcomas

Coordinator: Dr Frédéric Chibon

Specific themes
Sarcoma | Differentiation | Diagnosis | Genome | Oncogenesis | Prognosis | Chromosome | Metastasis | Hybrid tumor cell | Mitosis | Treatment | Heterogeneity

PROJETS

· **Oncogenesis of sarcomas** – Coordinator: Dr Frédéric Chibon – More info

FOCUS 2021

The level of genetic instability correlates with tumor aggressiveness in sarcomas

There is still no consensual chemotherapy for treating soft tissue sarcomas. In recent decades, research has focused on identifying patients with very aggressive tumors based on molecular or histologic signatures. The main hypothesis is that the more aggressive a tumor is, the more the patient can benefit from chemotherapy. The ONCOSARC team has previously shown that an intermediate level of genetic instability (GI) is associated with an increased risk of metastatic relapse in sarcoma compared to a low or high level.

The team has developed a new statistical method to measure GI based on the enrichment of mutations and breakpoints in defined tumor DNA motifs. The potential response to chemotherapy is thus better estimated. The team has demonstrated that patients with low GI would benefit the least from chemotherapy, and that it would even be detrimental to their prognosis, whereas patients with an intermediate or high level of instability could benefit from it. Read the article

A patent application has been filed. The creation of a start-up to commercialize a decision support software for clinicians is also under study.

→ Discover the team's publications

IRIT@CRCT

‘Michel Laudet’ digital oncology laboratory

Coordinators: Dr Jean-Marc Alliot, Dr Hervé Luga, Dr Sylvain Cussat-Blanc and Dr David Simoncini

Specific themes
Artificial Intelligence | Data analysis | Deep learning | In silico models | Computational design

PROJETS

· **Observance** – Coordinators: Pr Etienne Chatelut and Dr Joseph Gergaud – More info

· **Histopathological diagnostics** – Coordinators: Dr Camille Franchet and Dr Sylvain Cussat-Blanc – More info

· **3DCare Project** – Coordinators: Pr Pierre Brousset & Dr Hervé Luga – More info

· **LAM** – Coordinators: Dr Sarah Bertoli & Dr David Simoncini – More info

· **Modeling of molecular interaction maps** – Coordinators: Dr Sarah Bertoli & Pr Gilles Favre – More info

· **Immuno5 Project** – Coordinators: Dr Sylvain Cussat-Blanc & Dr Salvatore Valitutti – More info

· **Viro5D Project** – Coordinators: Dr Pierre Cordelier & Dr Sylvain Cussat-Blanc – More info

· **NanoCoDe Project** – Coordinators: Dr Aurélien Olichon & Dr David Simoncini- More info

· **PISA Project** – Coordinators: Dr David Simoncini, Dr Sylvain Cussat-Blanc, Dr Hervé Luga & Dr Pierre Cordelier – More info

FOCUS 2021

Creation of the first digital cancer research laboratory

At the beginning of April, the CRCT and the Toulouse Institute for Research in Computer Science (IRIT) announced the creation of the first digital cancer research laboratory. It was named «Michel Laudet» in honor of the famous Toulouse computer scientist who founded the CIT (Toulouse Computer Center) in 1963 and became the first president of IRIA (now INRIA) in 1967. Collaboration started five years ago with the SIGNATHER team (Pr Gilles Favre & Dr Olivier Sordet) from the CRCT to design a software for modeling signaling pathways (P3M project). This partnership now numbers 10 researchers from IRIT and 12 researchers from CRCT and IUCT-Oncopole, 2 PhD students, 3 post-docs and 5 trainees from the Grandes Ecoles (Polytechnique, INSA Toulouse, Ecole Centrale Paris and Ecole des Mines).

→ Discover the team’s publications

DETAILS PER ORGAN

Coordination Committee (OCC)

Gynecology OCC

Coordinator: Dr Laurence Gladieff

Main collaborations:
T2i team at the CRCT (Coordinator: Pr Maha Ayyoub), ONCOSARC team at the CRCT (Coordinator: Dr Frédéric Chibon) and Cellular Biophysics team at the IPBS (Laurent Paquereau)

EXPERTISE IN RARE TUMORS

The Oncopole is accredited as a «Regional Expert Center for Rare Gynecological Malignant Tumors» by INCa.

Incorporation of two new studies
Investigator: Dr. Laurence Gladieff
BOUQUET (Hoffmann-La Roche)
This international study is evaluating the efficacy and safety of biomarker-based therapies in patients with rare chemotherapy-resistant ovarian epithelial tumors (NCT04931342)
PembroSCCOHT (ARCAGY-GINECO)
This national trial is investigating the role of immune checkpoint inhibitors (IKIs) in a very rare but particularly severe ovarian cancer: hypercalcemic small cell carcinoma (NCT04602377).

RESEARCH IN SURGERY

Participation in national and international studies
Investigator: Dr Gwenael Ferron
SENTICOL III (Besançon University Hospital)
In 2021, final enrollment for this international validation study of sentinel node mapping in the surgical management of early cervical cancer (NCT03386734).
OVHIPEC-2 (The Netherlands Cancer Institute)
The objective of this study launched in April 2021 is to prove that intraperitoneal chemohyperthermia improves the outcome of primary cytoreductive surgery in FIGO stage III epithelial ovarian cancer (NCT03772028).
CHRONO (ARCAGY-GINECO)
This study seeks to determine the best moment to perform surgery, either during or after primary chemotherapy, in advanced ovarian cancers (NCT03579394).

ROLE OF IMMUNOTHERAPY

Participation in national and international studies
HUMMINGBIRD (ARCAGY-GINECO)
Investigator: Dr. Sarah Bétrian
In 2021, the final enrollment took place for this French pilot study evaluating, among other things, the immune impact and safety of nivolumab in combination with ipilimumab prior to initial chemoradiotherapy for treating advanced cervical cancer (NCT04256213).
KEYNOTE B21 / ENGOT-EN11 / GOG3053
Investigator: Dr. Laurence Gladieff
Launched in 2021, this study is evaluating the role of first-line immunotherapy in endometrial cancer (NCT04634877). A similar study for cervical cancer is ongoing (NCT04221945).
TEDOVA (ARCAGY-GINECO)
Investigator: Dr. Laurence Gladieff
Also launched in 2021, this study is comparing maintenance treatment with a vaccine alone or in combination with an immune checkpoint inhibitor (ICI) to standard treatment after chemotherapy for sensitive relapsed ovarian cancer (NCT04713514).

Hematology OCC

Coordinator: Pr Christian Récher

Main collaborations:
NoLymIT team at the CRCT (Coordinator: Pr Camille Laurent), GENIM team at the CRCT (Coordinators: Pr Hervé Avet-Loiseau & Dr Ludovic Martinet), IGAALD team at the CRCT (Coordinator: Pr Eric Delabesse) and METAML team at the CRCT (Coordinator: Dr Jean-Emmanuel Sarry)

JACIE & CAR-T CELL ACCREDITATIONS

The CCO Hematology is accredited JACIE (Joint Accreditation Committee of ISCT-Europe and EBMT) for hematopoietic cell transplantation and cell therapy. Since 2019, it has also been accredited for the use of Car-T cells in several indications: diffuse large B-cell lymphoma, acute lymphoblastic leukemia, myeloma and mantle cell lymphoma, with 27 patients treated with this innovation in 2021.

PRESENTATION OF DATAML TO THE SFH

Coordinator: Pr Christian Récher
The presentation of the work on the DATAML registry was one of the highlights of the 41st congress of the French Society of Hematology (SFH). Launched in 2009 by Prof. Christian Récher in collaboration with Prof. Arnaud Pigneux of Bordeaux University Hospital, DATAML is a registry that collects data from 4,900 patients with acute myeloid leukemia. Collaborations with international groups are also underway. The database is regularly searched in the context of research projects aimed at optimizing medical practices (more than 40 publications since its creation). New databases on graft and molecular biology data in connection with DATAML are under construction. More information

LAUNCH OF THE IALYMPH PROJECT

Coordinators: Pr Camille Laurent, Pr Pierre Brousset, Pr Loïc Ysebaert
A partnership has been signed with Laboratoires ROCHE as part of the IALYMPH project, which aims to identify predictive factors for response or recurrence using artificial intelligence approaches in lymphoma patients treated at the IUCT-Oncopole. The agreement represents €1.5 million for the period 2021-2025.

MM: PRECISION MEDICINE

Coordinators: Pr Jill Corre & Dr Aurore Perrot
In collaboration with the GENIM team at the CRCT, the Hematology CCO has shown that del(17p) testing is essential for the diagnosis and identification of high-risk patients (Blood publication). Other research conducted by the team has evaluated the efficacy of daratumumab alone (JCO publication) or in combination with lenalidomide (JCO publication).

FUNDING OF THE THEMIS PROJECT

Coordinator: Pr Loïc Ysebaert
As part of the development of the AMA (Assistance Malades Ambulatoires) nursing follow-up program, the THEMIS project evaluates the medico-economic impact of the coordination of nursing in patients with chronic lymphocytic leukemia treated with targeted therapies (NCT0535082). A grant of 880,000 euros was obtained in 2021 as part of the PRME medico-economic research program launched by the Ministry of Social Affairs and Health.

Neuro-oncology OCC

Coordinators: Pr Elizabeth Moyal & Dr Delphine Larrieu-Ciron

Main collaborations:
Team RADOPT at the CRCT (Coordinator: Pr Elizabeth Moyal), Team T2i at the CRCT (Coordinator: Pr Maha Ayyoub) and Team DEVIN (Coordinator: Dr Patrice Péran) at UMR Inserm 1214-ToNIC (Toulouse NeuroImaging Center)

STRATEGIC DIRECTIONS

The CCO is developing integrated research aimed at optimizing the management of brain tumors by studying radioresistance phenomena, optimization by ballistics and better definition of target volumes by multimodal imaging, as well as the prediction of therapeutic response thanks to blood, tumor and imaging biomarkers. The IUCT-Oncopole is an international referral center for neuro-oncology because of the innovative trials it promotes or participates in, particularly phase I-II trials.

STERIMGLI, SI2GMA & PIRAT

Coordinator: Pr Elizabeth Moyal

STERIMGLI is a nationwide (phase I/II) trial of the combination of stereotactic re-irradiation with immunotherapy that was launched in 2016. The phase I study evaluated the safety of the combination of hypofractionated stereotactic radiation therapy (hFSRT) and anti-PD-L1 immunotherapy (durvalumab) in patients with relapsed glioblastoma. Enrollment is now underway for the phase II trial to assess the efficacy (overall survival) of the combination therapy in recurrent glioblastoma (NCT02866747).

The **SI2GMA project** (*Stereotactic Irradiation and Immunotherapy Glioblastoma Markers*) is based on data from STERIMGLI and was the winner of the ARC Foundation's first call for SIGN'IT projects. It stems from collaboration with the radiotherapy department, the medical physics department, the pathology department, the T2i and RADOPT teams at the CRCT and the Grenoble Neuroscience Institute.

Another area of collaboration via the PIRAT (*Personalized Intelligent Radiotherapy*) study is the prediction of therapeutic response based on multimodal data from this clinical trial with AI researchers from the IRT Saint-Exupéry.

LAUNCH OF EPENDYMOMICS

Coordinator: Pr Anne Laprie

Winner of a PRTK in 2021, this project uses AI to combine imaging, dose therapy and molecular imaging (multiomics approach) to understand why 50% of children with ependymoma relapse. It is a collaborative projects between the IUCT-Oncopole radiotherapy department, the ToNIC/UMR1214 laboratory, the pathology departments of IUCT-Oncopole, Marseille and Paris-Saint-Anne, as well as LATIM UMR 1101, the Pasteur Institute and all French pediatric oncology centers (NCT05151718).

ANALYSIS OF A POLA COHORT

Coordinators in Toulouse: Pr Elizabeth Moyal and Pr Emmanuelle Uro-Coste

The IUCT-Oncopole developed a national study based on the POLA cohort (Affymetrix and clinical data) that aimed to compare the response to radiotherapy + chemotherapy with temozolomide to radiotherapy + PCV chemotherapy in patients with IDH-mutated anaplastic astrocytoma, both treatments being proposed as therapeutic options. The findings in favor of the latter strategy were published in 2021. Read the publication

Oncodermatology OCC

Coordinators: Pr Nicolas Meyer & Dr Dimitri Gangloff

Main collaborations:
MELASPHINX team at the CRCT (Coordinators: Dr Bruno Ségui and Dr Nathalie Andrieu)

SPECIFIC THEMES

The CCO Oncodermatology is one of the few national entities to offer treatment for all neoplastic pathologies such as lymphomas, carcinomas and melanomas. In addition, the IUCT-Oncopole is a member a) of CARADERM, the hospital network accredited by the INCa for rare skin cancers, e.g. Merkel's carcinoma, adnexal carcinoma and basal cell carcinoma; and b) of CAREPI, the hospital network accredited by the INCa for advanced squamous cell carcinomas.

ENCADO: EUROPEAN TASK FORCE FOR ADVERSE REACTION MANAGEMENT

Coordinator: Dr Vincent Sibaud
Working in collaboration with the Federico II University Hospital in Naples and the Fuenlabrada University Hospital in Madrid, Dr. Vincent Sibaud has set up the first task force exclusively dedicated to the management of adverse dermatological events related to cancer treatments. The task force called ENCADO (European Network for Cutaneous Adverse events to Oncologic Drugs) is composed of 73 dermatologists from 21 countries, including 18 European countries.

SURGICAL SPECIFICITIES

The IUCT-Oncopole is also one of three French centers to perform lymph node transfer, an innovative corrective surgical technique to treat refractory lymphedema practiced by Dr. Karim Kolsi since 2018. A medical thesis under the direction of Dr. Thomas Méresse was completed in 2021 to study the oncologic safety of perforator flap reconstruction surgery, an innovative technique that truly takes into account the anatomy and functionality of the areas and could replace the common practice of direct structural excision.

TRANSLATIONAL RESEARCH

Coordinator: Pr Nicolas Meyer
In collaboration with the CRCT teams, research focuses on the remodeling of the inflammation due to melanoma to improve the effectiveness of immunotherapy, and on the biomarkers of response to melanoma treatments.

PUBLICATION OF EARLY PHASE TRIAL RESULTS

In 2021, the results of an early phase study coordinated by Prof. Nicolas Meyer and Dr. Bruno Ségui, and published in Clinical Cancer Research, suggested that adding antibodies targeting the TNF cytokine to immune checkpoint inhibitors reduces the extent of side-effects. The therapeutic cocktail also appears to be very well tolerated by patients with advanced melanoma. Read the publication
Another phase I study led by Prof. Céleste Lebbé from AP-HP and piloted by Prof. Jean-Pierre Delord found that pimasertib has clinical activity in patients with locally advanced or metastatic melanoma, particularly with BRAF- and NRAS-mutated tumors, and at clinically relevant doses associated with inhibition of pERK in peripheral blood mononuclear cells Read the publication

Oncogenetics OCC

Coordinator: Pr Rosine Guimbaud

Main collaborations:
DIAD team at the CRCT (Coordinator: Pr Etienne Chatelut) and Pathology and Molecular Biology of Tumors platform (Coordinator: Pr Pierre Brousset), EQUITY team UMR1295-CERPOP (Coordinators: Dr Michelle Kelly-Irving & Dr Cyrille Delpierre) and REVA team at the IRIT (Coordinators: Dr Sylvain Cussat-Blanc & Dr Géraldine Morin)

STRATEGIC DIRECTIONS

The Oncogenetics CCO covers the oncogenetic needs of the Occitanie Ouest region thanks to the following: a) organizing genetic consultations and analyses at the IUCT-Oncopole site; b) holding regional multidisciplinary consultation meetings (RCP); c) conducting pre-consultations in the cities of Rodez and Tarbes; d) organizing training; and e) coordinating local care for genetically predisposed people in the region.

REGIONAL COORDINATION

The CCO collaborates closely with the IUCT-Purpan, the IUCT-Rangueil/Larrey and the Onco-Occitania network in order to offer follow-up programs for breast-ovarian syndromes, Lynch syndrome, familial adenomatous polyposis and hereditary endocrine neoplasia.
Headed by the Oncogenetics CCO, the GENEPY network (under the aegis of Onco-Occitania) facilitates and coordinates the implementation of optimal local care in the Occitanie Ouest region thanks to collaboration between the oncogenetics team at the Oncopole and professionals working in public or private hospitals or as private consultants.

MATADOR PROJECT

Coordinator: Dr Christine Toulas
Launched in 2021, MATADOR (Male breAsT cAncer preDisposition factOR) is a collaborative project involving the LBMO oncogenetics laboratory, and the EQUITY (UMR1295 - CERPOP) and REVA (IRIT) teams. Its ambition is to identify new predictive factors of breast cancer in men (MBC). The first steps of the project consisted in the analysis of sequencing data from a panel of 591 genes involved in cancer to search for genetic predisposition factors (other than the panel routinely used in the laboratory for breast and/or ovarian cancer predisposition syndrome, i.e. the HBOC panel) that may be responsible for an increased risk of breast cancer in men. The variants obtained in 85 MBC patients were compared with data from the general population (specifically with a control cohort of male subjects without cancer). The analysis revealed 20 pathogenic variants significantly more present in the MBC cohort than in the control cohort, within 15 genes of interest.
Funding was granted by the Regional Cancer League in late 2021 to perform some of the exome sequencing.

Oncogeriatrics OCC

Coordinators: Dr Loïc Mourey & Dr Laurent Balardy

The Oncogeriatrics OCC is part of the Midi-Pyrenees Oncogeriatrics Coordination Unit (UCOG), which functions in close collaboration with the Geriatrics Department at Toulouse University Hospital, and the Onco-Occitania cancer network.

ASSESSING THE CONSEQUENCES OF AGE

The Oncogenetics CCO covers the oncogenetic needs of the Occitanie Ouest region thanks to the following: a) organizing genetic consultations and analyses at the IUCT-Oncopole site; b) holding regional multidisciplinary consultation meetings (RCP); c) conducting pre-consultations in the cities of Rodez and Tarbes; d) organizing training; and e) coordinating local care for genetically predisposed people in the region.

REGIONAL COORDINATION

Impact of comprehensive geriatric assessment
Coordinator: Dr Laurent Balardy
This retrospective study published in the European Journal of Hematology showed that comprehensive geriatric assessment (CGA) has a real impact on decision-making in patients over 65 years of age. Analysis of patient characteristics over a 10-year period suggests that functional and motor impairment, comorbidities and age are predictive of changes in treatment plans. Read the article

Launch of the LYMPHOLD trial
Coordinator: Dr Laurent Balardy
Funded by the Ligue Contre le Cancer, this prospective cohort study conducted at the IUCT-Oncopole will evaluate the impact of chemotherapy on the functional autonomy and quality of life of patients aged 75 years and older treated for malignant hemopathies (NCT05101759).

End of inclusions for FRACTION
Coordinator: Dr Laurent Balardy
This project, which is funded by a PHRC-K, is investigating frailty and body composition in elderly subjects treated with chemotherapy for cancer. The objective is to establish how these factors impact their tolerance to chemotherapy. The ambition is to modify the current decision algorithms for the treatment of elderly cancer patients (NCT02806154).

FOCUS: ACUTE CONFUSIONAL SYNDROME

Evaluation of teaching practices
Dr Loïc Mourey & Dr Laurent Balardy
Launched in 2020, the MOOC «Cancer in the Elderly: better understanding its specificities for better care» is a project that is co-organized by the two UCOG in Occitania. In view of the frequency, severity and diagnostic and therapeutic difficulties encountered by health professionals when dealing with acute confusional syndrome (ACS), a MOOC module has been entirely devoted to it. The work gave rise to a paper in 2021 describing and evaluating professional pedagogical practices concerning the development and evaluation of the content of a MOOC module. Read the article

PRESIDENCY OF DIALOG

In the last year, Dr Loïc Mourey has been elected co-president of the French Oncogeriatrics Research Intergroup DIALOG with Pr Florence CANOUI-POITRINE (Epidemiologist Henri Mondor Créteil Hospital). Its accreditation by INCa has been renewed for 5 years. Its main objectives are to federate, facilitate and innovate to promote research in Oncogeriatrics. For more information

Oncopediatrics OCC

Coordinators: Pr Anne Laprie, Pr Marlène Pasquet & Dr Marie-Pierre Castex

Main collaborations:
IGAALD team at the CRCT (Coordinator: Pr Eric Delabesse), IRIT@CRCT team (Coordinator: Dr Jean-Marc Alliot) and DEVIN team (Coordinator: Dr Patrice Péran) at UMR Inserm 1214-ToNIC

SPECIFIC THEMES IN RADIOTHERAPY

Investigator: Pr Anne Laprie

End of the EPENDYMOMICS-TOX study

This project seeks to optimize the indications for proton therapy and to allow clinicians to choose the optimal treatment for ependymoma by minimizing sequelae and by improving the analysis of follow-up imaging so that post-therapy monitoring can be optimized. The results were presented at ESTRO and PROS in 2022.

Launch of the EPENDYMOMICS project

This project uses artificial intelligence to combine imaging, dose therapy and molecular imaging (multiomics approach) in an attempt to understand why 50% of children with ependymoma relapse. The Oncopole pathology department, the LATIM UMR 1101, the Institut Pasteur and all French pediatric oncology centers are collaborating on this project, which was awarded a PRTK of 793 k€ in 2021 (NCT05151718).

End of inclusions for IMPALA

This exploratory study is investigating the impact of different radiation doses received by children treated with radiotherapy on their cognitive functions related to the hippocampus and cerebellum. The analysis of the results, in This project run in collaboration with the ToNIC/UMR1214 laboratory and the University of Marseille (for the Markov models) will make it possible to finetune radiotherapy doses to regions involved in the development of cognition and memory (NCT04324450)

SPECIFIC THEMES IN CHEMOTHERAPY

BEACON (Univ Birmingham)
Investigator: Dr Marion Gambart

This international study led by the University of Birmingham is evaluating the value of combining an anti-VEGF monoclonal antibody with a standard chemotherapy regimen in children with relapsed or refractory neuroblastoma. Enrollment ended in 2021 (NCT02308527).

CURALASE01 (Toulouse University Hospital)
Coordinator: Pr Marlène Pasquet

Involving 18 treatment centers in France, this study was launched in May 2021 and aims to evaluate the modalities of administrating low-energy laser, an innovative treatment to relieve pain related to chemo-induced mucositis in children. It is funded by a PHRC-K (NCT04596410).

TRANSLATIONAL RESEARCH

Coordinator: Pr Marlène Pasquet

Discovery of a new GATA2 anomaly

The discovery of a previously undescribed GATA2 abnormality in a patient from Toulouse was the subject of a scientific publication in Blood in 2021, in collaboration with a team from Newcastle. Read the publication

Financing of the INTERPEDIA project

The objective of this INCa-funded project is to decipher the hematological phenotype of patients with the GATA2 mutation thanks to new models that better evaluate the leukemic risk and the role of allograft. The project is the result of collaboration with the IRIT@CRCT team and the IGAALD team at the CRCT. More about this project

Ear, Nose and Throat OCC

Coordinators: Pr Sébastien Vergez & Dr Anouchka Modesto

Main collaborations:
Team T2i et the CRCT (Coordinator: Pr Maha Ayyoub), Team RNAreg at the CRCT (Coordinator: Dr Stefania Millevoi) and Laboratory CIRIMAT – UMR CNRS INPT UPS 5085 (Coordinator: Pr Christophe Laurent)

Several ENT CCO physicians are members of GETTEC, the Head and Neck Tumor Study Group, as well as GORTEC, the Head and Neck Radiotherapy Oncology Group.

A FIRST IN EUROPE

Personalized vaccine TG4050
Investigator: Pr Jean-Pierre Delord
The first non-viro-induced ENT cancer patient to benefit from Transgene's TG4050 vaccine in Europe is a patient at IUCT-Oncopole, who was included in the phase I clinical trial launched in 2021. TG4050 is a personalized cancer vaccine that aims to induce a durable immune response in addition to active treatments, and to prevent relapse. (NCT04183166)

LYMPH NODE INVOLVEMENT

Ongoing inclusion in N-PARO
Coordinators: Pr Sébastien Vergez & Pr Agnès Dupret-Bories
Promoted by GETTEC, this project is evaluating the prevalence of lymph node metastases from primary parotid carcinomas, and the functional and oncologic outcomes of their surgical management (ID-RCB: 2020-A01247-32).

3D INNOVATION AND BIOMATERIALS

Coordinator: Pr Agnès Dupret-Bories
Creation of a 3D workshop
In partnership with the National Polytechnic Institute of Toulouse, the CIRIMAT laboratory and the 3D Medelab company, a 3D workshop was created in 2021 in the Department of Surgery. In particular, it allows cutting guides to be created for maxillofacial surgery.

Two ANR projects: BIOFISS & CongOs!
Prof. Agnès Dupret-Bories received ANR funding in 2021 for two projects:
› **The BIOFISS project** that she is coordinating, and which aims to develop an alga-based biomaterial for the prevention of salivary fistulas in cervico-facial surgery, in partnership with CIRIMAT, the INSERM 1121 unit in Strasbourg and two industrialists, Rescoll and Brothier Laboratories.
› **The CongOs project**, headed by CIRIMAT, where she is in charge of one of the work packages. The objective here is to develop a new porous composite material with antibacterial and angiogenic properties for bone reconstruction following mandibular osteoradionecrosis.

AI FOR DETECTION

Launch of the IA-LOPM project
Coordinators: Dr Emmanuelle Vigarios & Dr Delphine Comtesse-Maret
An innovative collaboration was launched at the end of 2021 with IRIT, ENSEEIHT and CRCT. The objective is to create an AI tool to assist in the diagnosis of oral lesions. The first step will be to develop clipping software that allows around 10,000 photos taken by the oral medicine department at the IUCT-Oncopole to be prepared for diagnostic purposes. For more information

Sarcoma OCC

Coordinator: Dr Christine Chevreau

Main collaborations:
Working closely with the ONCOSARC team at the CRCT (Coordinator: Dr Frédéric Chibon)

EXPERTISE

The IUCT-Oncopole is an expert sarcoma center and a bone referral center for the INCa-certified NETSARC+ network. Several physicians are involved in the European consortium FOSTER (osteosarcoma) and EuroEWING (Ewing's sarcoma).

SPECIFIC THEMES IN RADIOTHERAPY

Adaptive radiotherapy: Results
Coordinator: Dr Anne Ducassou
A project no completed that evaluated the value of preoperative adaptive radiotherapy to treat limb sarcomas. The results were presented as part of a medical thesis and are the subject of publications submitted in 2022.

MEDISARC-RS: CLIP² Innovative molecules
Coordinator: D. Thibaud Valentin
This phase I trial is one of the three winners of the CLIP² Innovative Molecules INCa-AstraZeneca 2021 call for projects. It will evaluate the safety of a bispecific anti-PD1/anti CTLA4 antibody in combination with stereotactic radiotherapy in patients with metastatic sarcoma. More about this project

SPECIFICITY IN SURGERY

PERFOSARC database
Coordinator: Dr. Thomas Méresse
Analysis of this database launched in 2020 allowed the assessment of the reliability of pedicled perforator flaps in reconstructive surgery for limb and wall soft tissue sarcomas in adults. Read more

Comparison of neoadjuvant treatment modalities in soft tissue sarcoma
Coordinator: Dr. Justine Attal
The results of this study assessing the value of concomitant neoadjuvant radiochemotherapy in patients with grade 2-3 soft tissue sarcoma were published in 2021. View article

TRANSLATIONAL RESEARCH

Coordinators: Dr Thibaud Valentin & Dr Frédéric Chibon

End of the SAMHY 1 study
The objective of this pilot study is to evaluate the rate of circulating tumor cells derived from fusion with macrophages, a mechanism potentially associated with metastatic spread (NCT04512495).

Continuation of the PHRC K and PRTK 2018 studies
Trial CHIC- STS 01 (PHRC-K 2018)
This multicenter study is evaluating perioperative chemotherapy in patients with localized grade 1 or 2 soft tissue sarcomas defined as high risk by CINSARC, a molecular signature identified in 2010 by Dr. Frédéric Chibon and now used routinely (NCT04307277).
MIRAS - SARRA (PRT-K 2018)
This is multicenter translational cohort study is seeking to establish the clinical and biological characteristics of rare soft tissue sarcomas (NCT04459234).

Launch of the GERICO 14 project
Coordinator: Dr. Thibaud Valentin
This randomized phase III study is comparing oral cyclophosphamide to doxorubicin in patients 65 years or older with advanced or metastatic soft tissue sarcoma. Read more

Senology OCC

Coordinators: Pr Florence Dalenc, Pr Charlotte Vaysse & Dr Eva Jouve

Main collaborations:
DynACT team at the CRCT (Coordinator: Dr Salvatore Valitutti), SIGNATHER team at the CRCT (Coordinators: Pr Gilles Favre & Dr Olivier Sordet), ONCOSARC team at the CRCT (Coordinator: Dr Frédéric Chibon) & «Cancer and Adipocyte Microenvironment» team at UMR 5089 CNRS IPBS (Coordinator: Pr Catherine Muller)

TWO MAIN TRANSLATIONAL THEMES

Metabolism and cancer
Coordinator: Pr Charlotte Vaysse
The objective is to characterize the role of adipocytes surrounding the tumor in cancer progression and the molecular mechanisms involved in obesity. One of the ongoing projects with Dr. Camille Franchet concerns the extensive characterization of mammary adipose tissue in breast cancer.

Mechanisms of resistance to PARPi
Coordinator: Pr Florence Dalenc
A prospective national cohort of patients treated with PARPi was initiated in 2021 to test whether POLQ expression (as well as other proteins involved in DNA double-strand break repair) by tumor cells can account for primary or acquired resistance to PARPi, and whether it varies with BRAC1 and/or 2 mutations.

AI PROJECT: APRIORICS

Coordinator: Dr Camille Franchet
Dr Camille Franchet, who is a pathologist, is coordinating the APRIORICS project (Immunohistochemistry Enhanced Deep Learning for Image Requalification of Breast Cancers) supported by the Health Data Hub and BPi France. The objective is to collate a large collection of richly annotated microscopic images of breast cancers (tumors and microenvironments), thanks to the development of an automatic annotation technique for immunohistochemically labeled images. This collection will then be used to train an algorithm that will lead to the launch of a precision tool to assist pathologists.

RESULTS OF THE PADA-1 STUDY

Investigators: Pr Florence Dalenc & Dr Anne Pradines
Promoted by Unicancer, PADA-1 (NCT03079011) is the first worldwide study using liquid biopsies to monitor the appearance of ESR1 mutations in circulating tumor DNA during first-line metastatic treatment with an anti-aromatase and palbociclib before disease progression. The results, which were presented at the San Antonio Breast Cancer Symposium (SABCS) 2021, demonstrate the efficacy of switching to fulvestrant after detection of an ESR1 mutation in circulating tumor DNA.

LAUNCH OF PRÉCIDIVE

Coordinator: Pr Charlotte Vaysse
Officially declared a national Health Innovation Project for 2021, PRéCIDIVE aims to prevent the recurrence of severe chronic disease by changing diet and promoting physical activity. It focuses on three diseases: gestational diabetes, COPD and breast cancer. For oncology, the study led by Prof. Florence Dalenc and Prof. Charlotte Vaysse concerns obese patients with non-metastatic breast cancer after the end of (neo)-adjuvant treatments.

Supportive Oncology Care OCC

Coordinators: Dr Nathalie Caunes-Hilary & Pr Virginie Woisard

Main collaborations:
IFERISS-CRESCO team (Coordinator: Pr Thierry Lang) and BIOETHICS UMR1027 team (Coordinator: Sandrine Andrieu)

FIGHT AGAINST PAIN

Opening of the TEC-ORL study
Coordinator: Dr Antoine Boden
This multicenter randomized phase II trial aims to evaluate the value of Qutenza in the management of patients in remission from ENT cancer but with persistent neuropathic pain. It is funded by PHRCI and its protocol was presented in a poster at the 13th AFSOS congress and published in BMC Cancer (NCT04704453).

Integration in two national studies
Experimentation of cannabis for medical purposes (ANSM)
Investigator: Dr Antoine Boden
Oncopole is the referral center for this study which will be launched in March 2021. Its focus is intractable symptoms related to cancer or its treatments, which account for 1/3 of the inclusions for this indication. Read more
KETACANCER (Léon Bérard Center, Lyon)
Investigator: Dr Valérie Mauries-Saffon
Launched in 2021, this prospective, multicenter observational study aims to evaluate the use of ketamine in the treatment of chronic refractory pain within the network of French cancer centers. (NCT04459234)

EVALUATE NEW MODELS

ARC funding of the TELEMSOS study
Coordinator: Dr Valérie Mauriès
Conducted in collaboration with the Inserm UMR1295 team (Dr. Bettina Couderc) and the Groupe de Recherche et d'Analyse des Populations en Santé (GAP - Dr. Sébastien Lamy), this project is investigating the contribution of telemedicine consultations conducted by the Mobile Pain and Palliative Care Team in the follow-up of patients suffering from chronic cancer. In 2021, the ARC granted 25 k€ for this project. More about this project

OPENING UP TO THE HUMANITIES

Exploration of ethical issues
Coordinator: Bettina Couderc
Advance directives
Thanks to funding from the INCa, the Ligue Contre le Cancer and the GSK Laboratory, the team launched a legal, sociological and psychological study in oncology in 2021. It concerned the possibility for French people to draft their advance directives in application of the relevant paragraphs of the Claeys-Léonetti law. More about this project
Deep sedation
In 2021, end of the project «Sociological and ethical reflections on the use of palliative sedation and medicalized end of life among professionals in the field of cancerology», financed by the ARC and the Ligue Contre le Cancer. More about this project

Signature of the GIS Parolothèque agreement
Coordinator: Pr Virginie Woisard
The agreement called Groupement d'Intérêt Scientifique (GIS) Parolothèque was signed between the Toulouse University Hospital, the Claudius Regaud Institute, the CNRS, the National Polytechnic Institute of Toulouse, and the universities of Toulouse, Avignon and Aix-Marseille. The objectives are to establish a corpus of voices and verbatim accounts of cancer patients, which can then be analyzed and studied in terms of speech and discourse. More about this project

Thyroid and neuroendocrine tumors OCC

Coordinators: Pr Rosine Guimbaud, Pr Frédéric Courbon and Pr Delphine Vezzosi

Main collaborations:
DIAD team at the CRCT (Coordinator: Pr Etienne Chatelut), INOV team at the CRCT (Coordinators: Dr Marc Poirot & Dr Sandrine Silvente-Poirot) and i2MC UMR 1048 Inserm/Université Paul Sabatier (Director: Dr Dominique Langin)

STRATEGIC DIRECTIONS

The Thyroid and Neuroendocrine Tumor CCO comprises researchers and staff from various units.
Neuroendocrine tumors (NETs) involve the collaboration of the Digestive Department at IUCT-Rangueil/Larrey, the nuclear medicine and pathology services of the IUCT-Oncopole, the Endocrinology Department at IUCT-Rangueil/Larrey, and the Biology Department at IUCT-Purpan.
Thyroid pathology concerns the endocrinology, ENT surgery and thoracic surgery departments at Toulouse University Hospital, as well as the nuclear medicine and ENT surgery departments at IUCT-Oncopole.

NATIONAL AND INTERNATIONAL EXPERTISE

Several members of this CCO are part of the National Study Group for Endocrine Tumors (GTE) as well as the INCa ENDOCAN reference network in its three branches: RENATEN (NET), TUTHYREF (thyroid cancers) and COMETE (adrenal cancers). Dr Slimane Zerdoud is a member of the Thyroid Committee of the European Association of Nuclear Medicine (EANM).
The CCO functions as a network between the IUCT-Oncopole and Toulouse University Hospital, and is one of only four French centers of excellence certified by the European Neuroendocrine Tumor Society (ENETS). This accredited center is called the Toulouse University Center of Excellence for Neuroendocrine Tumors. Dr Lawrence Dierickx is the coordinator and Prof. Rosine Guimbaud is the director.

EPILUNET REGISTRY

Coordinator: Pr Frédéric Courbon
EPILUNET (Epidemiology Lutetium NeuroEndocrine Tumor) is a national registry of Vectorized Internal Radiation Therapy (VIRT) of endocrine tumors by 177Lu DOTATATE (Lutathera®), which is funded by the SFMN and the CNP of nuclear medicine. It also receives technical and legal support from the Federation of Medical Specialties. EPILUNET differs from a database and a cohort in that it is exhaustive, unbiased and not limited in time.

NATIONAL ADVANCED NON-DIGESTIVE NET COHORT

Coordinator: Pr Rosine Guimbaud
In 2021, Prof. Rosine Guimbaud launched a national cohort of advanced non-digestive neuroendocrine tumors treated with chemotherapy.

Urology OCC

Coordinators: Pr Bernard Malavaud, Dr Loïc Mourey & Dr Jonathan Khalifa

Main collaborations:
T2i team at the CRCT (Coordinator: Pr Maha Ayyoub) & «Sphingolipids and cancers» team at the IPBS (Coordinator: Dr Olivier Cuvillier)

RECOGNIZED EXPERTISE

National reference center for human cancers
The IUCT-Oncopole is an INCa-certified regional reference center for prostate brachytherapy. The IUCT-Oncopole also initiated the national multidisciplinary 'testicular' meetings under the leadership of Dr Christine Chevreau.

Active member of cooperative groups
The team's strong involvement in learned societies such as the Association Française d'Urologie (AFU) and in cooperative groups such as GETUG (Groupe d'Etude des Tumeurs Uro-Génitales) allows the IUCT-Oncopole to have access to clinical trials of the same scientific level as North American and other European trials.

Pioneer in endoscopic bladder dissection
The CCO Urology team is an international pioneer in endoscopic monobloc bladder dissection techniques and is one of the few French teams performing third-generation cryotherapy rescue techniques.

EPILUNET REGISTRY

Coordinator: Dr. Jonathan Khalifa

Main research focus
Overall, the research conducted by the radiotherapy team focuses on the role of radiotherapy in metastatic stages, in addition to pain relief. Their general hypothesis is a paradigm shift to radiotherapy offered as standard treatment for stage IV disease.

Preliminary results of FDALO-RAD01
The phase II BLAD-RAD01 trial, which was awarded an INCa PHRC-K grant, is evaluating adjuvant radiotherapy for metastatic urothelial carcinoma of the bladder in partial or complete response after first-line systemic therapy (NCT04428554). The retrospective data were presented at ASCO 2021.

Department of Internal Medicine

Coordinator: Pr Odile Rauzy

Main collaborations:
METAML team at the CRCT (Coordinator: Dr Jean-Emmanuel Sarry), EQUITY team at the CERPOP (Coordinators: Dr Michelle Kelly-Irving & Dr Cyrille Delpierre), PEPSS team CIC 1436 (Coordinator: Dr Maryse Lapeyre-Mestre)

MISSIONS

The Internal Medicine Department has several missions within the Oncopole and Toulouse University Hospital. It is a referral center for the management of myelodysplastic syndromes (therapeutic trials, associated dysimmune manifestations). It also provides expertise in rare immuno-hematological diseases. In addition, it coordinates the management of infections in immunocompromised patients in oncology/hematology and complications related to immunotherapy. It is involved in non-programmed care, e.g. downstream of the emergency room and at the internal medicine and acute care day hospital.

MYELODYSPLASTIC SYNDROMES

Coordinator: Dr. Thibault Comont

Creation of a luspatercept registry

In 2021, the Oncopole contributed to the national evaluation registry of this innovative treatment for low-risk, transfusion-dependent myelodysplastic syndrome, which will become available in the summer of 2022.

Immune profile of myelodysplasias

The analysis of the immune profiles of patients with myelodysplastic syndrome, which was the subject of a doctoral thesis in collaboration with the CRCT, points to a link with leukemic transformation and the potential interest of these profiles for therapeutic screening.

Vexas syndrome

Since 2020, a research focus at the Oncopole has been inflammatory manifestations associated with hemopathies, in particular Vexas syndrome. The first publications are expected in 2021. Dr. Thibault Comont is also a member of the group that created the French Vexas Registry (phenotype and molecular).

RARE IMMUNO-HEMATOLOGICAL DISEASES

The internal medicine department is one of the four national reference centers for autoimmune cytopenia in adults (CeReCAI). It is also a center of competence for sickle cell syndrome, thalassemic syndrome and other rare red blood cell and erythropoiesis pathologies, hereditary immune deficiency and histiocytosis. To accompany patients with rare diseases on their care pathway, accompaniment consultations have been set up with the pediatric immunohematology team. A therapeutic patient education program for sickle cell patients was launched in 2021.

HEMOGLOBIN DISEASES

Coordinator: Dr Pierre Cougoul

In 2021, the IUCT-Oncopole became an observation center for the coexistence of sickle cell disease and onco-hematological pathology (SICKLONE working group). The department also took part in a pharmaco-epidemiological research project on the harmful effects of corticosteroids in sickle cell patients that was launched by the PEPSS team at the Clinical Investigation Center (CIC) 1436. The year 2021 also saw the end of the ACTIVATE industrial trial (NCT03548220) to evaluate the efficacy of the drug mitapivat, as well as the launch of the ESCORT-HU 2 study (NCT04707235).

Technical medical units

Department of Surgery

Head of department: Pr Sébastien Vergez
Deputy Head: Pr Alejandra Martínez

INNOVATIVE EQUIPMENT AND TECHNIQUES

The department includes 1 block with 7 operating rooms, 2 conventional hospitalization units (50 beds) and 1 ambulatory surgery unit (15 places). Thanks to a partnership with Olympus, one of the rooms in the block has 3D facilities. Hyperthermic intraperitoneal chemotherapy, bone reconstruction assisted by 3D printing, intraoperative radiotherapy (for breast cancer), and focal cryotherapy (for prostate cancer) are all innovative techniques deployed in the department.

PAROLA PROJECT: WINNER OF A PHRC

Coordinator: Professor Alejandra Martínez
Under the aegis of ARCAGY-GINECO and the *European Network of Gynecological Oncological Trial Groups* (ENGOT), this project is the second largest international study in gynecological cancer surgery after SENTICOL. PAROLA (*PARa-aOrtic LymphAdenectomy in Locally Advanced Cervical Cancer*), which was awarded PHRC-K funding in 2021-2022, is a phase III study that is examining the impact of curettage to adapt radiotherapy fields in cervical cancer (NCT05581121).

METHODOLOGY OF EXTENSION ASSESSMENT: RESULTS OF A STUDY

Coordinators: Pr Alejandra Martinez & Dr Erwan Gabiache
In 2021, the results of a study conducted in collaboration with the Department of Medical Imaging were published that compared extension assessments obtained by metabolic mapping by PET-scan with the Sugarbaker peritoneal index (PCI score). 8F-FDG PET/CT measurements proved highly accurate in reflecting the peritoneal tumor burden, with a diagnostic value that varies depending on the anatomical region.

LAUNCH OF A PERSONALIZED PHARYNGEAL STENT PROJECT

Coordinators: Pr Agnès Dupret-Bories & Dr Emilien Chabrillac
The year 2021 also saw the launch of a project to develop a new pharyngeal stent for the treatment of pharyngeal stenosis after total (pharyngo)-laryngectomy. The aim is to design customized pharyngeal stents to reduce pain and avoid the frequent expulsion of the stents currently used in patients undergoing total laryngectomy. This entire project, from the design of the prosthesis to the clinical trial, will be conducted in collaboration with the Lyon-based Innovative Technology Platform (ITP) 3d.FAB, the Novatech SA company and the startup 3Deus Dynamics.

Medical Imaging Department

Head of department: Pr Frédéric Courbon
Deputy Head: Pr Nicolas Sans

Main collaborations:
RADOPT team at the CRCT (Coordinator: Pr Elizabeth Moyal), General Electric Healthcare

The department is composed of **a radiology unit, a radiology-senology unit and nuclear medicine facilities** consisting of a radiopharmacy unit and an inpatient sector for internal vectorized radiotherapy.

INTERNATIONAL REFERENCE CENTER

European accreditation
The department's PET unit is EANM Research Ltd-accredited by the European Association of Nuclear Medicine (EANM). In addition, the IUCT-Oncopole and the IUCT Rangueil/Larrey have joined forces to form the Toulouse Neuroendocrine Tumor University Center of Excellence, which is accredited by the European Neuroendocrine Tumor Society (ENETS).

World Validation Center
Coordinators: Pr Frédéric Courbon and Dr Olivier Caselles
The IUCT-Oncopole Imaging Department is also General Electric HealthCare's world validation center for their new generation of PET scanners, which will be installed at IUCT-O in 2022.

CONTINUATION OF INCLUSIONS FOR GENEBIOLUNET

Coordinator: Dr. Lavinia Vija Racaru
The GENEBIOLuNET project, which is supported by the GIRCI-SOHO, consists in measuring the variability of molecular biomarkers that can characterize radionuclide therapies (Lu-177 DOTATATE) in patients with metastatic midgut neuroendocrine tumors (NCT03667092).

IMPACT OF MULTIPARAMETRIC MRI IN EVALUATING TUMOR BURDEN

Coordinators: Pr Alejandra Martinez & Dr Erwan Gabiache
In 2021, the results of a study conducted in collaboration with the Department of Medical Imaging were published that compared extension assessments obtained by metabolic mapping by PET-scan with the Sugarbaker peritoneal index (PCI score). 8F-FDG PET/CT measurements proved highly accurate in reflecting the peritoneal tumor burden, with a diagnostic value that varies depending on the anatomical region.

END OF INCLUSIONS FOR MEDIRAD

Investigator: Pr Frédéric Courbon
The department is a partner in the H2020 MEDIRAD (Implication of MEDIcal low-dose RADiation exposure) project launched in 2017. Coordinated by ISC Global (Spain) and the University of Paris Descartes, MEDIRAD is a consortium of 33 partners from 14 European countries whose aim is to federate the scientific and medical communities in the field of research on medical radiation protection, and to optimize the use of ionizing radiation in radiotherapy, nuclear medicine, medical imaging and interventional radiology. Medical applications include the use of iodine 131 for the treatment of thyroid cancer. The IUCT-Oncopole is the only partner that is undertaking clinical research (NCT03986437).

Department of Medical Physics

Director: Dr Laure Vieillevigne
Co-director: Grégory Hangard

Main collaborations:
RADOPT team at the CRCT (Coordinator: Pr Elizabeth Moyal)

RADIOTHERAPY EQUIPMENT

The department has four types of equipment: 3 tomotherapy machines (Accuray) including 1 'new generation' Radixact, 1 linac (Varian), 2 True Beam Novalis (Varian) and 1 Halcyon (Varian). At the end of 2021, IUCT-Oncopole became one of the first centers to be equipped with a KV tube to drive its Radixact (Accuray) (Investigator: Marine Stadler). This new feature improves the quality of repositioning imaging while reducing acquisition time and delivered doses. The year 2021 was also marked by the implementation of the HyperArc technique (Varian) in September (Investigator: Eliane Graulières).

MULTICENTER STUDY ON SMALL-FIELD DOSIMETRY: RESULTS

Coordinator: Dr Laure Vieillevigne
A working group of the French Society of Medical Physicists (SFPM) was created to collect small field aperture collimator factors. The objective of the study coordinated by Dr Vieillevigne was to collect and disseminate information on these factors for various clinical stereotactic radiotherapy equipment and measurement configurations. A total of 23 centers participated in this study. See the article

GAMMORA: DEVELOPMENT OF AN AUTOMATIC SIMULATION SOFTWARE

Coordinator: Dr Luc Simon
GAMMORA is an open-source simulation tool (LGPL license) developed in collaboration with the CRCT RADOPT team to easily generate Monte-Carlo GATE simulations for radiotherapy with the Novalis TrueBeam system. The results of this work, which benefited from access to the CALMIP supercomputer (project 2016-P19001) and support from the INCA (STEREPID grant), is available in open access: https://github.com/uhqd/GAMMORA

DEVELOPMENT OF A METROLOGY FORMALISM BASED ON MONTE-CARLO SIMULATIONS

Coordinator: Dr Laure Vieillevigne
No international dosimetric protocol exists to transform the signal of a detector into a dose in a medium other than water. To address this issue, a formalism has been developed by the CRCT RADOPT team. It uses Monte-Carlo simulations on the GATE platform and has been validated experimentally on the Novalis True Beam at the Oncopole. The project was made possible thanks to access to the CALMIP supercomputer (project P22004). See the article

SUPPORT FOR THE IMPLEMENTATION OF CARDIAC STEREOTAXIS

Investigator: Thomas Brun
The department has partnered Dr Jonathan Khalifa (radiotherapist at the IUCT-Oncopole) and Dr. Philippe Maury (cardiologist at Rangueil-Toulouse University Hospital) in implementing cardiac stereotaxy at the IUCT-Oncopole. Refractory ventricular tachycardia is treated by stereotactic irradiation. The first patient was treated with this innovative treatment in June 2021, followed by three others during the year.

RADIOTHERAPY EQUIPMENT

Coordinators: Aurélie Tournier, Dr Luc Simon
In 2021, the department signed a partnership agreement with the company Vision RT, which markets an SGRT (Surface Guided Radiation Therapy) system, for the provision of an SGRT module for stereotactic procedures. The objective is to evaluate the contribution of a surface system for such procedures. The results were presented at the Journées de la Société Française de Physique Médicale in 2021.

Radiotherapy Department

Coordinator: Pr Elizabeth Moyal

Main collaborations:
with the RADOPT team at the CRCT (Coordinator: Pr Elizabeth Moyal)

Since its creation in 2018, the Radiotherapy Department has been highly involved in the INCa network RADIOTRANSNET, which focuses on preclinical radiotherapy research. Prof. Moyal is also a member of the scientific committee.

RECOGNIZED EXCELLENCE

State-of-the-art facilities
The IUCT-Oncopole was the first center in France to use adaptive tomotherapy. It also possesses Halcyon technology, which features a particle accelerator and a scanner and optimizes image-guided radiotherapy with intensity modulation at all levels. In 2021, the department received HyperArc technology. In total, the department possesses all the latest techniques in radiotherapy thanks to its eight recent complementary devices. In collaboration with the Engineering and Medical Physics Department, dosimetric studies are conducted to determine the most appropriate device according to the patient's pathology and clinical condition.

OECI Award
During the audit carried out as part of the Comprehensive Cancer Center accreditation in 2020, the Organization of European Cancer Institutes (OECI) considered that among the many sites audited over the previous five years, the IUCT-Oncopole radiotherapy department was an example in terms of quality and safety of care and integrated research.

A WINNING COMBINATION

Choosing the right chemotherapy
To improve the management of IDH-mutated anaplastic astrocytomas, the Department of Radiation Therapy, in collaboration with the Department of Pathology, conducted a study on the national POLA cohort to determine the best chemotherapy protocol following radiation treatment for this disease. For the first time, this study demonstrated the clinical benefit of the PCV (procarbazine, lomustine and vincristine) combination administered after radiotherapy.

A FIRST IN TOULOUSE

When radiotherapy is used in cardiology
For the first time at the IUCT-Oncopole, a patient suffering from a recurrent cardiac rhythm disorder, ventricular tachycardia refractory to classic therapies, was treated by radiotherapy. Stereotactic radiotherapy, which is usually used in cancerology, was used to destroy a cardiac zone responsible for the tachycardia. The procedure was made possible thanks to close collaboration between the radiotherapy teams of Prof. Elizabeth Moyal at the IUCT-Oncopole and the rhythmology teams of Pr Philippe Maury and Dr Anne Gardères-Rollin at Toulouse University Hospital - Rangueil. The first three patients were treated with this technique in 2021.

Medical Biological Oncology Laboratory (LBMO)

Coordinator: Pr Gilles Favre

Main collaborations:
Three teams at the CRCT share Coordinators with the MBOL: Prof. Gilles Favre (Team SIGNATHER), Prof. Etienne Chatelut (Team DIAD), and Prof. Maha Ayyoub (Team T2i).

MAIN ACTIVITIES

The LBMO, which 98% COFRAC-accredited, is organized into five sectors:
·Rapid response biology (Coordinator: Dr Laurence Malard)
·Pharmacology (Coordinator: Pr Etienne Chatelut)
·Immuno-monitoring (Coordinator: Pr Maha Ayyoub)
·Oncogenetics and pharmacogenetics (Coordinator: Dr Christine Toulas)
·Prospective biology (Coordinator: Dr Anne Pradines)

RESULTS OF THE TICE STUDY

Coordinators: Pr Etienne Chatelut & Dr Christine Chevreau
The Pharmacology team participated in the TICE phase II study, the results of which were published in 2021. This study concerning patients with malignant germ cell tumors aimed to evaluate the impact a new therapy based on high-dose chemotherapy consisting of two cycles combining paclitaxel and ifosfamide, and three cycles of high-dose carboplatin associated with etoposide for 3 days. Thanks to subtle management of drug dosing, significant efficacy was observed with satisfactory tolerance. See the publication

RESULTS OF THE PADA-1 STUDY

Investigators: Dr Anne Pradines & Pr Florence Dalenc
Since 2018, the prospective biology unit has been using digital PCR to analyze ESR1 mutations in circulating tumor DNA, in the PADA-1 study carried out by Unicancer and the GINECO group (NCT03079011). For the first time, results show that early detection of the ESR1 mutation in circulating DNA in patients treated with an aromatase inhibitor and an anti-CDK4/6 drug allows early adjustment of hormone therapy with fulvestrant before clinical progression, and thus significantly prolongs survival without disease progression. Nearly 1,000 first-line patients with HER2-positive metastatic breast cancer receiving palbociclib and letrozole were included in the PADA-1 study. These highly innovative results presented at the San Antonio Breast Cancer Symposium (SABCS) 2021 raise the question of the routine monitoring of circulating DNA. Clinical trials using this strategy are ongoing.

ACQUISITION OF THE CELLSEARCH® SYSTEM

In late 2021, the LBMO acquired the CELLSEARCH® system, an automated reference platform for the identification, enrichment and enumeration of circulating tumor cells, as well as circulating endothelial cells from a single blood sample. CELLSEARCH® is the only system approved by the *Food & Drug Administration* (FDA). This acquisition will enable the development of innovative projects based on the detection and phenotypic and molecular characterization of circulating cells.

Oncohematology Laboratory

Coordinator: Pr Véronique De Mas

Main collaborations:
IGAALD team at the CRCT (Coordinator: Pr Eric Delabesse), GENIM team at the CRCT (Coordinator: Pr Hervé Avet-Loiseau & Dr Ludovic Martinet), METAML team at the CRCT (Coordinator: Dr Jean-Emmanuel Sarry) and IRIT@CRCT Michel Laudet team (Coordinator: Dr Jean-Marc Alliot)

A WELL-KNOWN LABORATORY

The Oncohematology Laboratory possesses two platforms: the automated technical platform (ATP) and the specialized technical platform in hematology (STP). The STP includes the Hematology Genetics Unit (all liquid hemopathies except myeloma) and the Myeloma Genomics Unit (only myeloma).
The laboratory is a reference unit for the GRAALL (Adult Acute Lymphocytic Leukemia), CAALL-F01 (Childhood Acute Lymphocytic Leukemia) and IFM (Intergroupe Francophone du Myélome) protocols.

AI PROJECTS

The creation of the IRIT@IUCT-O team in 2021 has given rise to two projects in collaboration with the oncohematology laboratory:
·A project, led by Dr Sarah Bertoli and Dr David Simoncini, consists in digitizing diagnostic myelograms of acute myeloid leukemia (AML) (2,000 adult patients) and developing tools for cell labeling by AI with the search for prognostic markers, in collaboration with the Hematology CCO. More about the project
·Using the same principle, another project led by Dr Marlène Pasquet will characterize GATA2 patients according to phenotypic, molecular and genetic criteria. More about this project

A WINNING COMBINATION

Investigator: Pr Christian Récher
The Oncohematology Laboratory created the molecular and cytogenetic profiles for this study (NCT00590837) evaluating the value of adding lomustine to induction therapy in patients with AML. The results were published in 2021 in Leukemia. See the article

FAMILIAL AND GENETIC HEMOPATHIES

The laboratory has collaborated in several projects on familial and genetic hemopathies, including two projects with results published in 2021: a study on PAX5 germline mutations (see the article) and another on GATA2 germline mutations (see the article).

MULTIPLE MYELOMA: PROGNOSIS CONFIRMED FOR 'DOUBLE HIT'

A study coordinated by Pr Hervé Avet-Loiseau, Pr Jill Corre and Pr Aurore Perrot on a population of 121 patients compared to a cohort of 2,500 patients without a deletion on the short arm of chromosome 17, confirmed the expected results: the so-called 'double hit' phenomenon, i.e. a del(17p) associated with mutations on the TP53 gene corresponds to the worst diagnosis (median survival = 36 months) However, the deletion alone is a very high-risk feature since it is associated with a median survival of 52.8 months (compared with 152.2 months for the control population). These results confirm the prognostic value of del(17p). See the article

Pharmacy

Coordinator: Dr Jean-Marie Canonge
Deputy Head: Dr Florent Puisset

Main collaborations:
DIAD team at the CRCT (Coordinator: Pr Etienne Chatelut)

LEVERAGING ACCESS TO INNOVATION

Coordinator: Dr Anaïs Grand

Experimental MTI & Car-T-cells

The unit obtained ARS accreditation for the management of advanced therapy drugs in 2018 and for car-T-cells in 2019. In addition to the necessary equipment such as cryogenic storage rooms and a vacuum-controlled atmosphere area, the unit has set up a dedicated organization with a pharmacist whose role is to manage car-T-cells as well as two interns trained in advanced therapy drugs. The year 2021 was marked by the first inclusions for the trials on the personalized vaccine TG4050 against ENT (NCT04183166) and gynecological cancers (NCT03839524)

Home-nursing: A first in France

In collaboration with MSD Laboratories, the project to administer experimental injectable treatments at home - a first in France for cancerology - was initiated at the IUCT-Oncopole thanks to coordination between the care teams, the PUI's clinical research unit and the clinical investigation platform. The patient's care pathway was rethought, and the pharmacy teams reorganized to prepare the experimental treatment once it had been validated by the investigating physician, and to send it to the patient's home.

SPECIFIC RESEARCH

Coordinator: Dr Florent Puisset

Assessments in current practice

The IUCT-Oncopole pharmacy has the largest anticancer drug reconstitution unit in France (Clinical Oncology Pharmacy Unit), so it can handle large amounts of data on patient treatments. It is therefore able to evaluate drugs in current practice and in particular their dosages. In 2021, the results of an evaluation of the benefit/risk balance of brentuximab in routine practice, including in situations outside marketing authorization, were published (1) as well as the results of a study on the risk of overdosing with methotrexate in obese patients due to its dosage based on body surface area (2).

Focus on alternative therapies

In 2021, EUTACAM, a single-center prospective pilot study, was launched with the support of the Ligue Contre le Cancer. The objective is to evaluate the impact of alternative or complementary therapies on the therapeutic adherence of breast cancer patients treated with tamoxifen. A study on the impact of turmeric on the pharmacokinetics of tamoxifen is envisaged (NCT04740697)

Pathology platform

Director: Pr Pierre Brousset
Deputy directors: Pr Emmanuelle Uro-Coste & Pr Philippe Rochaix

Main collaborations:
NoLymIT team at the CRCT (Coordinator: Pr Camille Laurent) & DynAct team at the CRCT (Coordinator: Dr Salvatore Valitutti)

ORGANIZATION

Considered as one of the largest pathology laboratories in Europe in terms of activity, the unit is composed of five units:
·Conventional Histopathology (Coordinator: Dr Claire Illac)
·Cytology (Coordinator: Dr Celine Basset)
·Immunohistochemistry (Coordinator: Nathalie van Acker)
·Molecular biology (Coordinators: Pr Laurence Lamant, Pr Solène Evrard, David Grand & Frédéric Escudié (engineers)
·Digital imaging (Coordinators: Dr Camille Franchet, François-Xavier Frénois (engineer)

RECOGNIZED EXPERT CENTER

The platform is recognized as a regional expert center within the framework of INCa-labeled reference networks for four rare cancers: malignant pleural mesotheliomas and rare retroperitoneal tumors (Mesopath), soft tissue and visceral sarcomas (RRePS), rare neuroendocrine tumors (TENpath), and lymphomas (Lymphopath). For the latter, the laboratory is also the national coordinator with Créteil (12,000 cases per year). Thanks to its pathology platform, the IUCT-Oncopole is also one of the two European reference centers for the typing of amyloidosis (Coordinator: Dr. Magali Colombat).

SEVERAL AI PROJECTS IN PROGRESS

Several projects exploring the possibilities offered by Artificial Intelligence are underway:

APRIORICS
Coordinator: Dr Camille Franchet
This project aims to train AI to recognize tumors and their microenvironments from thousands of microscopic images of grade II breast cancers. The data (annotated virtual slides) will then be made available to the scientific community under an open-source license. Undertaken in collaboration with Thales, the project is funded by the Toulouse Cancer Excellence Laboratory (LabEx Toucan), the Foundation for Medical Research (FRM), the Health Data Hub and BPI France.

IALYMPH
Coordinators: Pr Pierre Brousset, Pr Camille Laurent & Pr Loic Ysebaert
In partnership with Roche Genentech, this project aims to use AI to identify predictive factors for response or recurrence in patients with diffuse large-cell B-cell lymphoma, based on the analysis of images obtained routinely. The aim is to use histological images processed by the pathology department, as well as images from PET scans, in collaboration with Dr. Salim Kanoun of the medical imaging department.

Biological Resource Center (BRC)

Coordinator: Pr Anne Gomez-Mascard

RECOGNIZED EXCELLENCE

The BRC has been ISO 9001 and NF-S-96 900 certified since 2020, thus enabling it to undertake projects of international scope. It was cited as one of the site's strong points in the OECI certification process (obtained in June 2020), as part of the IUCT-Oncopole's Comprehensive Cancer Center label.

NEW COLLECTIONS

The BRC possesses 23 collections, 13 of which were obtained from care provided at the Oncopole and 10 other hosted collections. This totals 140,000 samples (tumor and non-tumor). In 2021, 6 new collections became available:
>MICRO-BLAD: blood, urine, feces from bladder cancer patients (NCT04970472)
>INSPIRE: Collection of biomarkers of biological aging in mice (NCT04224038)
>Prospective multicenter cohort of digestive tumors with POLE/D1 mutation (block reception)
>CAPITOL: blood, fresh biopsies for paraffin-embedded blocks, and freezing (NCT04896684)
>COREC: samples from patients with chronic cough (NCT04882943)
>PHACS: blood from patients with breast tumors (NCT01127295)
The BRC also organized the arrival of the future HIMIP collection (Hematological Malignancies of Inserm Midi-Pyrénées)).

A FRUITFUL YEAR

In 2021, the BRC was involved in 57 research projects and 30 clinical studies. In addition, a dedicated specialist for project-specific clinical data research was recruited in 2021. More than 8,200 new samples were received at the BRC in 2021, and more than 9,800 requests for samples were dealt with by the team.

In addition, actions already ongoing have been continued:
>Creation of a block library (colon, lung, breast and kidney collections)
>Provision of fresh tissue in collaboration with the pathology platform
>Annotation of key collections including the INCa-BACAP pancreatic adenocarcinoma collection (NCT02818829).
>To better meet the needs of researchers on site, steps are being taken for the BRC to become the histopathology platform of the CRCT: dedicated personnel; purchase of additional equipment (stainer, dehydration machine).
>Continued collaboration with Pierre Fabre Laboratories and EVOTEC through several projects.

CRB Cancer IUCT
Centre de Ressources Biologiques

Resuscitation and Continuing Care Unit

Coordinator: Dr Guillaume Ducos

Main collaborations:
GrrrOH - Respiratory Research Group in Onco-Hematological Resuscitation (Coordinator: Pr Azoulay), METAML team at the CRCT (Coordinator: Dr Jean-Emmanuel Sarry)

PROSPECTIVE MULTICENTER STUDIES

PIC, DéPOH, CARTTAS projects
Investigator: Dr. Muriel Picard
The IUCT-Oncopole ICU is participating in two randomized multicenter studies - DéPOH (coordinator Dr Djamel Mokart, sponsor IPC Marseille, 2015-022) and PIC (coordinator Dr Virginie Lemiale, sponsor AP-HP, P150961) – which respectively are examining the impact on mortality at D90 of de-escalation of antibiotic therapy in hematologic cancer patients admitted to the ICU for septic shock or severe sepsis, and the impact on mortality of adding corticosteroid therapy to the treatment of severe pneumocystis in immunocompromised patients.
The department also participated in the international observational multicenter study CARTTAS on the prognosis of patients admitted to the ICU after administration of CAR T-cells (coordinator Pr Elie Azoulay, AP-HP sponsor).

INFLA-PCP study
Investigator: Dr. Sihem Bouharaoua
The department is also involved in local collaborations such as the INFLA-PCP study evaluating markers of the decrease in inflammation during Pneumocystis jirovecii infections (principal investigator Pr Elisabeth Berry, parasitology-mycology laboratory, promoter Toulouse University Hospital, RC31/18/0098).

MANAGEMENT OF HYPER-LEUKOCYTIC ACUTE MYELOID LEUKEMIA (AML)

Patients from the Occitanie Ouest region diagnosed with hyperleukocytic AML are initially managed in the IUCT-O intensive care unit because of potential fatal initial complications. The unit therefore works in close collaboration with the hematology department (Pr Christian Récher), the hematology laboratory (Pr Véronique De Mas, Dr François Vergez) and the METAML team at the CRCT (Dr Emmanuel Sarry) and has co-authored papers on several clinical and biological investigations.

POST-OPERATIVE MANAGEMENT OF MAJOR GYNECOLOGICAL CANCER SURGERY

The department also undertakes the postoperative management of patients undergoing heavy gynecological cancer surgery, with co-authorship of studies conducted by Dr Gwénaël Ferron on postoperative complications.

MANAGEMENT OF SEVERE COMPLICATIONS IN PATIENTS WITH SICKLE CELL DISEASE

Investigator: Dr Muriel Picard
The unit also collaborates with the internal medicine department at the IUCT-O, which is the regional reference center for the management of patients with sickle cell disease. The unit participated in a national retrospective study on the prognosis of these patients admitted to the ICU (coordinator: Dr Jean-Baptiste Lascarrou, promoter CHU Nantes).

Anesthesiology Unit

Coordinator: Dr Philippe Izard

MANAGING PAIN AND STRESS

ONCOPECS:
Coordinator: Dr Olivier Gilbert
This retrospective study compared the number of patients requiring morphine titration in the recovery room (ICU) after mastectomy and immediate prosthetic reconstruction with and without pectoralis major muscle nerve block (PECS1). The purpose of this study was to determine whether PECS 1 is associated with improved tolerance of a subpectoral prosthesis after mastectomy. The results were presented at the 2022 SFAR congress. More about this study

Participation in two new PHRC-K
Oncopole investigator: Dr Régis Fuzier
ER-One (Lorraine Cancer Institute)
Launch in 2021 of a randomized, non-inferiority, multicenter, double-blind clinical trial evaluating the effect of erector spinal block (ESP) versus paravertebral block (BPV) on acute pain after breast cancer surgery (NCT04827030)
COHEC2 (Montpellier Cancer Institute)
Awarded a PHRC-K in 2021, this phase III study aims to evaluate the impact of a non-medicinal intervention program using guided breathing at a fixed frequency (cardiac coherence) associated with medical hypnosis on pre-operative anxiety in cancer surgery (NCT05197972).

ANTICIPATING RISKS

Presentation of the results of the national survey on the implementation of Long-Term Intravenous Devices (LTID)
Coordinator: Dr. Claire Cabos
Entitled «Placement of long-term intravenous devices and bleeding risk: a national survey of cancer centers,» this study was launched in 2020 and was the subject of a paper at SFAR 2021.

Launch of collaboration with the IRT St-Exupéry
Coordinator: Dr Régis Fuzier
In 2021, a project was launched with the Saint Exupéry Institute of Technological Research (IRT) to design a tool to assist in making anticipatory therapeutic decisions, based on predictive indexes of the occurrence of intraoperative arterial hypotension (Coordinator: Dr Bertrand Combres). A formal collaboration agreement will be signed in 2022 and other projects will be launched in 2023.

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