FOCUS RESEARCH 2022

COLLECTIVE EXPERTISE TO **FIGHT CANCER**



CONTENTS

Impact & achievements

TOULOUSE CANCER RESEARCH
CENTER (CRCT)4

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Impact & achievements Key figures 2022

LESS THAN



MONTHS

for a discovery by the CRCT to be translated into a clinical trial at the IUCT-Oncopole

> 707 PUBLICATIONS

55 PUBLICATIONS

with an impact factor > 20

+4% compared to 2020 +83% in 5 years



177 RESEARCHERS

18 RESEARCH TEAMS

20 NATIONALITIES among the different researchers 118

ENGINEERS, TECHNICIANS, AND ADMINISTRATIVE PERSONNEL

> TECHNICAL RESEARCH PLATFORMS

LABORATORY OF EXCELLENCE:



ERC GRANT



European Research Council Established by the European Commission



340 CLINICAL TRIALS opened for inclusions in 2022

> 40% EARLY PHASE

> > **TRIALS**

1,855 NEW PATIENTS

included in 2022 (+6% compared with 2021)



as many clinical trials —a figure that has doubled since the creation of the IUCT-Oncopole **9 YEARS AGO**

16,5% of the active file of patients included in a clinical trial

INCLUSIONS

31% SPONSORED BY THE IUCT-ONCOPOLE

> **45%** SPONSORED BY ACADEMIA

24% SPONSORED BY INDUSTRY



DETAILS PER TEAM

Toulouse Cancer Research Center (CRCT)



Anti-tumor immunity and immunotherapy

Coordinators: Pr. Maha AYYOUB and Pr. Jean-Pierre Delord

Specific themes

Tumor antigen-specific T cells | T cell depletion | Immune checkpoint inhibitor immunotherapy | Clinical trials | Genomics | Transcriptomics | Orthotopic preclinical models | Anti-cancer vaccines

PROJETS



• Role of tumor antigen-specific T lymphocytes in clinical responses to immunotherapies and development of cancer vaccines - Coordinators : Pr Maha Ayyoub - <u>More info</u>

• Impact of tumor immune microenvironments on response to immunotherapies – Coordinator: Dr Christel Devaud – <u>More info</u>

• Immune complexity of epithelial cancers -Coordinator: Pr Alejandra Martínez and Dr Anna Salvioni - <u>More info</u>

 Setting up clinical trials and immune monitoring of patients treated with immunotherapy – Coordinator: Dr Clara-Maria Scarlata – <u>More info</u>

• **Targeting of autophagy in cancer immunotherapy** - Coordinator: Dr Sylvie Giuriato - More info FOCUS 2022



Using a preclinical orthotopic model of metastatic colorectal cancer, the T2i team demonstrated the systemic anti-metastatic effect of intestinal T lymphocytes capable of migrating to other organs. This finding was then validated in patients with colorectal cancer treated with immunotherapy. The team is continuing this work to define signatures predictive of response to immunotherapies and to develop anticancer vaccines aimed at boosting these intestinal T lymphocytes. Read article

The team pursued its work showing the role of depleted T cells as predictors of clinical response to immunotherapy. <u>Read article</u>

The team is currently taking part in two clinical trials designed to evaluate TG4050, the personalized cancer vaccine developed by Transgene. Launched in 2021, these trials concern gynecological and ENT cancers. The first non-viral-induced ENT cancer patients to benefit from this vaccine in Europe are IUCT-Oncopole patients. The T2i team has joined forces with the immunomonitoring platform to monitor these two innovative phase 1 clinical trials at the IUCT-Oncopole. To find out more



Microenvironment and therapeutic resistance in pancreatic neoplasms

Coordinator: Dr Corinne Bousquet

Specific themes

Pancreatic Cancer | Microenvironment & Cancer-associated Fibroblasts | Metastases | Chemoresistance Translational regulation Matrix rigidity & mechanotransduction Metabolic reprogramming Patientderived 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

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Research coordinated by Dr Corinne Bousquet and Prof Cindy Neuzillet (Institut Curie - Saint Cloud) based on bioinformatics and immunohistochemical analyses on a large number of patients with pancreatic adenocarcinoma has identified molecular signatures associated with different original subpopulations of cancer-associated fibroblasts, two of which are prognostic and help in defining specific subtypes of immune, anti-tumor or immuno-suppressive stroma. Identifying these stromal signatures could enable better molecular stratification of tumors and hasten personalized medicine in this cancer, which remains a therapeutic failure. Read the article



Discover the team's publications

Optimizing radiotherapy: 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 – <u>More info</u>

• Optimizing the determination of absorbed dose in external radiotherapy - Coordinator: Dr Laure Vieillevigne - <u>More info</u>

 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

• Predicting response to radiotherapy using Artificial Intelligence - Pr Elizabeth Moyal and Ahmad Berjaoui - More info FOCUS 2022



Metabolic shift & radioresistance

The MSrGB (*Metabolic Shift in radioresistance of Glioblastoma*) project, which is coordinated by Prof. Elizabeth Moyal and accredited by the Fondation ARC (PGA) in 2022, aims to study the involvement of metabolic shift in glioblastoma stem cells in adaptation and resistance to radiotherapy. In addition to the RADOPT team, this program involves the IUCT-Oncopole, as well as Prof. Tourneret's team at IRIT, where new metabolites and their ability to predict relapse after treatment will be identified and studied using *deep learning*. To find out more



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 - <u>More info</u>

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

- Coordinator: Dr Bastien Gerby - More Into

• 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 - <u>More info</u>

 Study of germline alterations of transcription factors in acute leukemia - Coordinator: Pr Dr Cyril Broccardo - <u>More info</u> 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. <u>Read</u> the article



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 | Memory-resident CD8+ T cells | Tumor microenvironment

PROJETS



• The struggle between cytotoxic T lymphocytes and tumor cells at the lytic synapse - Coordinator: Dr Salvatore Valitutti - <u>More info</u>

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

• Functions and regulation of tissue memoryresident 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

 Study of the functional heterogeneity of human CTL against cancer cells – Coordinator: Dr Brienne McKenzie – <u>More info</u>

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Advances in cytotoxic T lymphocyte function

lover the past year, the DynAct team's research has progressed along three main lines:

• In collaboration with the ATTACK consortium funded by the prestigious European ERC Synergy Grant, the team has helped characterize the lytic compartment of cytotoxic T lymphocytes (CTL). <u>Read article</u>

• The team has shed new light on the molecular mechanisms by which aggressive tumors such as melanoma resist CTL attack at the lytic synapse. Read the article

 In collaboration with Dr. Sylvain Cussat-Blanc (Institut de Recherche en Informatique de Toulouse - IRIT), the team has developed a new approach to instance segmentation in microscopy that takes advantage of the highly innovative application called Cartesian Genetic Programming (CGP) of biological images. A patent application has been filed for this program and an article has been submitted for publication (K. Cortacero et al, under revision).



Cellular signaling, oncogenesis and therapeutics

Coordinators: Pr Gilles Favre and Dr Olivier Sordet

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

· Transcription in oncogenesis and response to anti-cancer treatments - Coordinator: Dr Agnese Cristini - More info

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Development of a technique to identify RHO **GTPase inhibitors**

The SIGNATHER team has developed a new technique based on the coupling of phage display and green fluorescent protein fractionation (split-GPF) to identify intracellular antibodies capable of inhibiting RHO GTPase signaling. The team has used this technique to identify an intracellular antibody called RH28, which is capable of selectively inhibiting certain RHOs and their associated phenotypes in melanoma cells. This work paves the way for future therapeutic strategies based on the disruption of protein-protein interactions using intracellular antibodies. To find out more



RNA biology in hematological tumors

Coordinators: Dr Stéphane Pyronnet & Dr Fabienne Meggetto

This team is part of the Labex TOUCAN.

Specific themes mRNA translation | Non-coding RNA | miRNAs | IncRNAs | circRNAs | Reticulum stress | Acute leukemia | Pediatric T lymphoma | Oncogenesis | Treatment resistance | Targeted therapies | Biomarkers

PROJETS



 Translational control of gene expression in hematological tumors - Coordinator: Dr Stéphane Pyronnet - <u>More info</u>

• Regulation of microRNAs and circular RNAs and their theranostic potential in ALKassociated anaplastic large cell T lymphoma – Coordinators: Dr Fabienne Meggetto & Dr Laurence Lamant – <u>More info</u>

• 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-<u>More info</u> FOCUS 2022



L'Oréal-UNESCO Foundation Award

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. On Wednesday October 12, 2022, Loélia Babin was awarded one of the 35 Prix Jeunes Talents 2022 from the L'Oréal-UNESCO Women in Science Foundation for her research on circular RNAs. <u>Read more</u>



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 | Enzymology | Pharmacology | 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 - <u>More info</u>

 Study of signaling pathways activated by oncosterone and dendrogenin A - Coordinator: Dr Sandrine Silvente-Poirot - <u>More info</u>

• New probes for non-invasive tumor detection by medical imaging - Coordinator: Dr Philippe de Medina & Pr Frédéric Courbon - <u>More info</u>

 Study of cholesterol metabolism deregulation in neuroendocrine cancers – Coordinator: Dr Lavinia
Vija – <u>More info</u> FOCUS 2022



Study of the mechanism of action of a cholesterol derivative that activates the immune system against tumors

The team, which has been accredited by the Ligue contre le cancer, studies the deregulation of cholesterol metabolism in various cancers, especially breast, thyroid and melanoma cancers. These translational studies have led to the discovery of a new metabolic branch in the cholesterol pathway, which in humans generates molecules involved in the progression or control of carcinogenesis. One of these molecules is dendrogenin A (DDA). After discovering that DDA is a cholesterol metabolite present in humans and mammals, the team demonstrated that it is a metabolite endowed with tumor suppressor properties, and that it has a chemopreventive effect in metastatic breast cancer and melanoma. In 2022, the team published a highimpact paper in the Journal of Extracellular Vesicles on the characterization of a fine mechanism involved in the anti-cancer action of DDA. It demonstrated that treatment with DDA modifies tumor cells, which become 'normal' and secrete small vesicles called exosomes, which in turn block tumor progression by activating the immune system against the tumor. This original mechanism throws much light on the physiological properties of DDA in its immunomonitoring action against cancer. The study was made possible thanks to funding from our institutions, the Ligue Contre le Cancer, the Institut National du Cancer, the Toulouse Cancer Santé Foundation and the generosity of the J'y Vais and Elles associations.



Integrated cellular signaling and PI3K isoforms

Coordinator: Dr Julie Guillermet-Guibert

Specific themes

Oncogenic signaling PI3Ks | Targeted therapies | Resistance | Tumor niche | Cancer initiation | Mechanobiology | Compression | Genetically modified mice | Tumor imaging | Pancreatic cancer | Ovarian cancer

PROJETS



Better diagnosis and treatment with targeted therapies - Coordinator: Dr Céline Basset - <u>More info</u>

• Importance of PI3K isoforms as a major factor in mechanotransduction – Coordinators: Dr Morgan Delarue and Dr Mickael Di-Luoffo – <u>More info</u>

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

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Cross-regulation between PI3Ks

Can they be used to better prevent tumor progression?

PI3Ks are a family of three classes of enzymes essential to cell life and which are frequently deregulated in cancer. The dependence of tumors on different types of class I PI3Ks is governed by putative genetic mutations and the tumor context (inflammation, etc.). While knowledge of class II and III PI3Ks in cancer is still too limited, class I PI3Ks seem to be dependent on mechanisms similar to those responsible for tumoral growth. The future of anti-cancer therapies targeting PI3Ks lies in a better understanding of these enzymes and the simultaneous targeting of several classes of PI3Ks with innovative drugs.

This project, coordinated by Dr Benoit Thibault and Dr Julie Guillermet-Guibert, will benefit in 2022 from the permanent recruitment of Dr Benoit Thibault as an Inserm researcher.

Discover the team's publications

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 - <u>More info</u>

 Modeling and simulation of cellular interactions in the tumor by individual-centered approaches – Coordinator: Dr Nina Verstraete – <u>More info</u>

• 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 – <u>More info</u>

 Epigenomics and chromatin networks -Coordinator: Dr Benoit Aliaga- More info

Chair in Oncology Bioinformatics

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 2022



Studying 3D DNA in the nucleus

The NetB(IO)² team has been studying the organization of DNA in 3D for many years, using analogies that represent DNA regions as nodes in a network that are connected if they are close together, just as a social network has links between people who know each other. This network is very important in the case of cancer, as cancer cells sometimes show alterations, not in the genes, but in the switches.

In a <u>recent paper</u>, the team used the network of connections between genes and switches, which can be viewed on the <u>GARDEN-NET</u> web, to identify a new biomarker in large T-cell lymphocytic leukemia. <u>Another application of this network analogy</u> enabled the team to discover how DNA replication – the process that makes one copy of DNA before the cell divides – is organized three-dimensionally, potentially exploiting the same organization used for gene regulation.



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 – <u>More info</u>

 Interconnections between TNF signaling and ceramide metabolism in melanoma – Coordinator:
Pr Bruno Ségui – <u>More info</u>

 Reprogramming ceramide metabolism to overcome resistance to immunotherapies -Coordinator: Dr Céline Colacios - <u>More info</u>

 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 - <u>More info</u>

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Discovery of new biomarkers of resistance to melanoma immunotherapies

The team showed that neutralization of TNF α , 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-TNF α 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.



New immunotherapies for lymphoma

Person in charge: Pr Camille Laurent

This team is part of the Labex TOUCAN.

Specific themes

Blymphoma/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

 \cdot Tumor microenvironment screening: tumor-associated macrophage blockade and T_{\gamma\delta} lymphocyte activation - Coordinator: Dr Mary Poupot - More Info

 Characterization and therapeutic targeting of a novel immunoregulatory mechanism – Coordinator: Dr Don Marc Franchini – <u>More info</u>

• 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





International Consensus Classification (ICC) of Mature Lymphoid Neoplasms.

Camille Laurent and Pierre Brousset have joined the ICC *Clinical Advisory Committee* to update the diagnostic criteria for mature lymphoid neoplasms. <u>Read the article</u>

NoLymIT is a partner in the European TRANSCAN-3 BIALYMPH project

The NoLymIT team is a partner of BIALYMPH in the European research program TRANSCAN, coordinated by Dr Wolfgang Huber and including five research teams: UKHD Heidelberg, two Inserm teams (MOBIDIC from Université de Rennes/Inserm and NoLymIT from CRCT). University of Palermo and Eotyos Lorand Research Network & Biological Research Centre. The objective is to identify patients with follicular B lymphoma who may or may not respond to bispecific antibodies. The NoLymIT team will characterize immuno-escape mechanisms using multi-omics approaches in the lymph nodes of FL patients from the various clinical trials of the three major European cooperative groups: German Lymphoma Alliance (GLA), French Lymphoma Study Association (LYSA), and Italian Lymphoma Foundation (FIL). To find out more



Myeloma oncogenomics and immunology

Coordinators: Pr Hervé Avet-Loiseau & Dr Ludovic Martinet

This team is part of the Labex TOUCAN.

Specific themes Multiple myeloma | Genomic changes | Clonal selection | Resistance | Immunity | Cytotoxic lymphocytes | Immune escape | Immunotherapy

PROJETS



 Molecular alterations and heterogeneity in myeloma cells - Coordinators: Pr Hervé Avet-Loiseau & Dr Jill Corre - <u>More info</u>

 Cytotoxic cell landscape controlling myeloma development and clinical outcome - Coordinator: Dr Ludovic Martinet - <u>More info</u>

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

 Finding new immunotherapeutic strategies for myeloma - Coordinator: Ludovic Martinet - <u>More info</u> FOCUS 2022



Robert A. Kyle Achievement Award

In June 2022, Prof. Hervé Avet-Loiseau was awarded the prestigious Robert A. Kyle *Achievement Award by the International Myeloma Foundation* (IMF) for his major contribution to the study of myeloma. The award is named after Dr Kyle, who was the first recipient of the award in 2002. In 20 years, only two other Frenchmen have received this award before Pr Hervé Avet-Loiseau. The IMF rewards research work based on the analysis of genetic/genomic abnormalities observed in malignant plasma cells, using a variety of techniques and technologies including fluorescence in situ hybridization (FISH), gene expression profiling, single-nucleotide polymorphism (SNP) chips and nextgeneration sequencing (NGS). <u>To find out more</u>



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 leukemia | 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

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In 2022, Dr. Jean-Emmanuel Sarry was awarded the Grand Prix Guy Lazorthes. All organisms adapt their metabolism in response to different types of stress in order to survive. This ability to respond metabolically to stress ensures heterogeneity and plasticity, leading to the emergence of cellular subpopulations with advantages in survival, proliferation and reconstitution of the original population. Jean-Emmanuel Sarry and his team have shown that this adaptive mechanism is a determinant of the therapy-resistant cancer cells responsible for relapse in many tumors. A better understanding of these metabolic adaptations should lead to new therapeutic solutions to overcome resistance. To find out more



Discover the team's publications

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 posttranscriptional control - Coordinator: Dr Stéphane Manenti - <u>More info</u>

 Link between RNA & autophagy – Coordinator: Dr Estelle Espinos – <u>More info</u>

 • RNA binding proteins, autophagy & response to therapies in HNSCC - Coordinators: Dr Stefania Millevoi & Pr Sébastien Vergez - More info FOCUS 2022



The RNAreg team, created by INSERM in 2021, brings together experts in the fields of protein synthesis (Stefania Millevoi and Anne Cammas), 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. The team's work published in 2022 documents the importance of non-canonical RNA structures in regulating protein synthesis (Herviou (2022) Methods Mol. Biol.) associated with glioblastoma proliferation and survival (LeBras (2022) Cancers; in collaboration with N. Skuli and B. Tyler at Johns Hopkins University School of Medicine, Baltimore, USA) as well as the role of PIM kinase in B cell differentiation, thanks to collaboration with T. Fest's team (Université de Rennes) which has opened up new therapeutic options in multiple myeloma (Haas (2022) Blood). Among the highlights of 2022, the team was accredited by the ARC Foundation for Cancer Research for three years to conduct a project aimed at characterizing the role and mechanism of action of RNA structures in energy metabolism. The team has also obtained funding from INCA (INCA PLBIO program) for three years in collaboration with S. Britton's team at IPBS and C. Joffre at CRCT to characterize a new function of the CHK1 protein in autophagy in response to genotoxic stress.



Discover the team's publications

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 – <u>More info</u>

 Oncoproteins and protein-protein interactions involved in therapeutic resistance - Coordinator: Dr Nicolas Bery - <u>More info</u>

• Mechanisms of infection by oncolytic viruses and new approaches to immunotherapy - Coordinators: Pr Louis Buscail & Dr Pierre Cordelier - <u>More info</u> FOCUS 2022



Pancreatic tumors are notorious for their resistance to immunotherapies. In this context, the ImPACT team has been investigating the therapeutic potential of Toll-like receptor (TLR) agonist molecules, which are expressed in tumors, and have shown antitumor activity in other contexts. In vitro, treatment with TLR7 agonists, and to a lesser extent with TLR2 agonists, inhibits growth and induces apoptosis in pancreatic cancer cells. This effect was observed in vivo, when tumor cells were implanted in the pancreas of immunocompromised mice. In contrast, administration of TLR7 agonists accelerates tumor progression in immunocompetent models of pancreatic cancer. This unexpected effect is due to a repolarization of the tumor microenvironment, and specifically to the presence of macrophages that support tumoral growth. These findings draw attention to the duality of action of TLR7 agonists in pancreatic cancer (PMID:35038581).

Inhibiting difficult-to-target proteins, such as those functioning through protein-protein interactions, with small molecules is a challenge owing to the lack of a well-defined catalytic pocket on these proteins. The team has established a protocol that is a generic method for discovering small molecules inhibiting the interaction between an intracellular antibody and its target. This protocol can be applied to any target or intracellular antibody. (PMID: 35340285).



Individualizing cancer drug doses

Coordinator: Pr Etienne Chatelut

Specific themes

Pharmacokinetics | Pharmacogenetics | Treatment individualization | Pharmacological therapeutic 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 colon cancer in the young (EXPECT) - Coordinator: Dr Christine Toulas - More info

• Oral therapies: Adapting oral anticancer drug dosages for patients unable to swallow-Coordinators: Coordinators: Dr Cécile Arellano & Dr Florent Puisset - <u>More info</u>

• Pharmacokinetic modeling of radiolabeled antibodies to understand resistance mechanisms in immunotherapy - Coordinator: Dr. Melanie White-Koning - <u>More info</u>

• Quantifying the sources of inter-individual variability in exposure to hormone therapy - 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 – <u>More info</u> FOCUS 2022



Theranostic radiolabeled molecules and the concept of optimal exposure

We are developing the concept of optimal plasma exposure, which is well known for 'classical' drugs, in the context of vectorized internal radiotherapy and in particular of177 Lu-Dotatate, a somatostatin analog prescribed for the treatment of endocrine tumors. We have shown that the nature of the amino acids administered simultaneously with this radiolabeled molecule to reduce renal toxicity has an impact on exposure to this drug. In general, we are studying the pharmacokinetic parameters of 177 Lu-Dotatate and their variability in two clinical trials: a phase 1 study in oncopediatrics and a study in adults investigating tumor radiosensitivity factors.



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 - <u>More info</u> FOCUS 2022

The level of genetic instability correlates with tumor aggressiveness in sarcoma

A molecular (or genomic) signature evaluates the expression of certain genes involved in the development and proliferation of a tumor, based on a tumor sample. These signatures can be powerful prognostic or predictive biomarkers. Discovered by Frédéric Chibon, CINSARC is a transcriptional signature derived from the expression of 67 genes involved in the control of mitosis and chromosome integrity. First identified in sarcoma, CINSARC has demonstrated its prognostic efficacy in many types of cancer.

The outcome of stage II-III colorectal cancer is highly variable, and the choice of treatment is currently based on the international TNM classification. However, studies show that some stage III patients have a better prognosis than some stage II patients.

In work published in collaboration with the pathology department at IUCT-Oncopole and the digestive oncology department at Toulouse University Hospital, the ONCOSARC team has shown that CINSARC significantly divides the patient population studied into two different groups, thus surpassing international standard classifications. Read the article



'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

 Histopathological diagnostics - Coordinators: Dr Camille Franchet and Dr Sylvain Cussat-Blanc

3DCare Project - Coordinators: Pr Pierre Brousset
& Dr Hervé Luga

• LAM - Coordinators: Dr Sarah Bertoli & Dr David Simoncini

 Modeling of molecular interaction maps -Coordinators: Dr Sarah Bertoli & Pr Gilles Favre

• Immuno5 Project - Coordinators: Dr Sylvain Cussat-Blanc & Dr Salvatore Valitutti

• **Viro5D Project** - Coordinators: Dr Pierre Cordelier & Dr Sylvain Cussat-Blanc

NanoCoDe Project - Coordinators: Dr Aurélien
Olichon & Dr David Simoncini

 PISA Project - Coordinators: Dr David Simoncini, Dr Sylvain Cussat-Blanc, Dr Hervé Luga & Dr Pierre Cordelier

FOCUS 2022



Improving deep learning of histological images

The choice of the optimal classification for a training data set is a key factor in the performance of a system based on deep-learning. This is especially the case for histological images used in cancer diagnosis, whose annotation requires the intervention of specialists in the field. Several hypotheses were tested by the team and led to results of interest, notably that natural classification produces more accurate results than artificially generated balanced classification. Results published in 2022 also suggest that multi-label examples are more useful than singlelabel ones for training a segmentation model, and that when the classification model is tuned from a balanced validation dataset, it is less affected than the segmentation model by the class distribution of the training set. See article



FOCUS RESEARCH 2022 / 23



DETAILS PER ORGAN

Coordination Committee (OCC)



Gynecology OCC

Coordinator: Dr Laurence Gladieff

Main collaborations:

<u>CRCT T2i team</u> (Coordinator: Pr Maha Ayyoub), <u>CRCT ONCOSARC team</u> (Coordinator: Dr Frédéric Chibon) and <u>Cellular Biophysics team at the IPBS</u> (Laurent Paquereau)

RARE TUMORS

The Oncopole is accredited as a Regional Expert Center for Rare Gynecological Malignant Tumors (TMRG) by INCa.

Open to TROPHAMET inclusions

Investigator: Dr. Laurence Gladieff

Supported by the Hospices Civils de Lyon, this phase 1-2 study aims to evaluate the safety and efficacy of avelumab in combination with standard methotrexate in patients with low-risk gestational trophoblastic tumors in first-line therapy (NCT04396223).

SURGERY



ESGO re-accreditation

Coordinated by Pr Alejandra Martínez with Drs Gwénaël Ferron and Laurence Gladieff, the European training program offered at the IUCT-Oncopole was re-accredited in 2022 for two *'training positions' by the European Society of Gynecological Oncology* (ESGO) over five years. Young European surgeons receive training in onco-gynecological surgery and take part in scientific activities, in collaboration with other CRCT teams.

PHRC-K funding for PAROLA

Coordinator: Pr Alejandra Martínez

PAROLA (PARa-aOrtic LymphAdenectomy in locally advanced cervical cancer) is an international trial conducted under the aegis of the GINECO, ENGOT and GCIG cooperating groups. The aim of this phase III study is to determine the role of lumbo-aortic lymph node dissection in locally advanced cervical cancer, and to evaluate new biological and radiomic biomarkers. It includes a medico-economic study between the participating European countries (NCT05581121).

IMMUNOTHERAPY, TARGETED THERAPIES



Participation in ARCAGY-GINECO studies

Investigator: Dr Laurence Gladieff

Launch of DOMENICA

This phase III study (NCT05201547) is comparing chemotherapy alone with dostarlimab in the first-line treatment of patients with advanced or metastatic endometrial cancer and DNA repair abnormalities (dMMR).

Launch of NIRVANA-1

This is a randomized trial comparing paclitaxelcarboplatin followed by maintenance with niraparib versus the same treatment plus bevacizumab in patients with high-grade, FIGO III stage ovarian, tubal or peritoneal cancer after initial complete cytoreduction surgery (NCT05183984).

SUPPORTIVE ONCOLOGY CARE



Closure of FEMINICOL trial

Coordinator: Dr Anne Ducassou

This single-center prospective study including 60 patients evaluated the impact of sexological nursing follow-up on sexual function in cervical cancer patients treated with radiotherapy and brachytherapy (<u>NCT03956498</u>). The results were presented as a short communication at the annual congress of the Société Française d'Oncologie Gynécologique (SFOG) 2022.

Hematology OCC

Coordinator: Pr Christian Récher

Main collaborations:

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

The OCC Hématologie is accredited for the use of Car-T cells, and is also JACIE-accredited (Joint Accreditation Committee of ISCT-Europe and EBMT) for hematopoietic cell transplantation and cell therapy.

MM: IMPACT OF DEL(P1P32)



Coordinators: Pr Hervé Avet-Loiseau & Pr Jill Corre

Work coordinated by Prof. Hervé Avet-Loiseau & Prof. Jill Corre on the cytogenetic abnormalities involved in multiple myeloma resulted in two prestigious publications at the end of 2022. The first confirmed the impact of the del(1p32) deletion on prognosis (see <u>article</u>). The second showed that these anomalies are present from the moment of diagnosis and often missed on mass analysis (see <u>article</u>).

RESISTANCE TO CAR-T CELLS



Coordinators: Pr Camille Laurent & Dr Charlotte Syrykh

CAR-T cells have revolutionized lymphoma treatment in recent years. However, the efficacy of this treatment is rarely long-lasting. Prof. Camille Laurent and Dr. Charlotte Syrykh have identified genetic remodeling as one of the possible explanations for this resistance to treatment. They have also identified acquired mutations in the PI3K and KRAS pathways that could be targeted by complementary therapies to overcome resistance to Car-T cells. <u>Read the article</u>

A COMBINATION BECOMES STANDARD TREATMENT



Coordinator: Pr Christian Récher

In collaboration with the Institut Gustave Roussy, the international Phase III AGILE trial is designed to evaluate the combination of azacitidine chemotherapy with a new targeted therapy, ivosidenib (a selective inhibitor of IDH1 mutant enzymes). The results, published in the New England Journal of Medicine, show that this combination therapy triples patient survival and is also better tolerated. Read the article

MM: LAUNCH OF VAMOS



Coordinator: Pr 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 (<u>Blood publication</u>). 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

Launched in June 2022 in collaboration with the AF3M association and the Onco-Occitanie network, the VAMOS (Vivre Avec un Myélome en Occitanie-oueSt) study is aimed at all newly-diagnosed multiple myeloma (MM) patients starting first-line treatment and living in the Occitanie-Ouest region. Over 1,600 patients will be included over the next five years and followed up until 2032. This real-life study aims to describe medical and paramedical practices in the region, study the care pathways of these patients, and collect data on patients' quality of life, as well as their feelings (NCT04888039).

Neuro-oncology OCC

Coordinators: Pr Elizabeth Moyal & Dr Delphine Larrieu-Ciron

Main collaborations:

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

PSEUDOPROGRESSION & RADIONECROSIS



Coordinator: Pr Elizabeth Moyal

Two of the team's articles were published in 2022 on MRI analyses of response to radiotherapy. The first, published in Biomedicines, focused on the phenomenon of pseudoprogression (see article). The second, published in Cancers, concerned radionecrosis (see article). The latter is part of the national SI2GMA project coordinated by Prof. Elizabeth Moyal, whose aim is to study which patients with recurrent glioblastoma would benefit from a well-tolerated combination of immunotherapy and radiotherapy.

MSRGB PROJECT: ARC ACCREDITATION

Coordinator: Pr Elizabeth Moyal

MSrGB aims to study and validate the involvement of metabolic shift in resistance to radiotherapy in glioblastoma. The study will be carried out on blood samples already collected as part of a trial, as well as on MRI spectroscopy data from the longitudinal follow-up of these patients. The *metabolome analysis* on the blood samples will be carried out by Dr. Laurent Debrauwer's team (INRAE Toulouse). Longitudinal analysis of new metabolites and their modifications on MRI spectroscopy will be carried out by Dr Lotfi Chaari (IRIT-ENSEEIHT) in close collaboration with Dr Soleakhena Ken from the CRCT's RADOPT team.

AI PARTNERSHIP WITH AIRBUS



Coordinator: Pr Elizabeth Moyal

A partnership between the IUCT-Oncopole and Airbus was signed in 2022. Two collaborative projects have already been launched:

• A failure prediction project, also in collaboration with a manufacturer

A project to optimize patient scheduling on different machines

Trainees are co-supervised by Airbus and IUCT-Oncopole.

PRELIMINARY RESULTS FROM IMPALA



Coordinator: Pr Anne Laprie

IMPALA is a study launched in 2020 in collaboration with the Inserm ToNIC (Toulouse NeuroImaging Center) team to investigate the impact of different radiation doses received by children treated with radiotherapy on their cognitive functions related to the hippocampus and cerebellum. The initial results were presented at the annual congresses of the Pediatric Radiation Oncology Society (PROS) and the International Society of Pediatric Oncology (SIOP).

OVERCOMING RESISTANCE TO METASTASIS



Coordinator: Pr Elizabeth Moyal, Dr Céline Dalmasso & Dr Aurore Siegfried

Published in the prestigious journal Nature Medicine, the Spanish team coordinated by Dr Manuel Valiente (CNIO), in collaboration with the radiotherapy and pathology departments of the IUCT-Oncopole and the onco-pneumology teams at Toulouse Rangueil University Hospital, have identified a biological pathway for resistance to radiotherapy in brain metastases. <u>See the article</u>

Oncodermatology OCC

Coordinators: Pr Nicolas Meyer & Dr Dimitri Gangloff

Main collaborations:

<u>CRCT MELASPHINX team</u> (Coordinators: Dr Bruno Ségui and Dr Nathalie Andrieu)

SPECIFIC THEMES



The Oncodermatology OCC 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.

In collaboration with CRCT teams, research focuses on the remodeling of the inflammatory environment of melanoma to improve the efficacy of immunotherapy, and on biomarkers of response to melanoma treatments.

INTERNATIONAL TASK FORCE TO MANAGE ADVERSE REACTIONS



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 European Task Force dedicated exclusively to the management of dermatological adverse events linked to cancer treatments. 120 dermatologists from 25 countries (18 of them European) are now involved: ENCADO stands for European Network for Cutaneous Adverse events to Oncologic Drugs. To combine forces and strengthen collaboration between this European group and its American counterpart, Dr. Vincent Sibaud has been appointed Chair of the International Committee for 2022, making him the only European representative on the board of the US Oncodermatology Society.

PRELIMINARY RESULTS OF ATTACK



The Oncodermatology OCC is taking part in the ATTACK project coordinated by Dr Salvatore Valitutti (head of the CRCT's DynAct team), and winner of the prestigious ERC (European Research Council) Synergy Grant. The project focuses on analyzing the tactical arsenal of lymphocytes in the fight against cancer. In a paper published in 2022, Dr Salvatore Valitutti's team explained how they used 'time-lapse' live-cell microscopy to obtain high-resolution spatio-temporal analyses of the events occurring at the lytic synapse between cytotoxic T lymphocytes and melanoma cells. They visualized a wave of calcium propagating through the tumor cell within milliseconds, triggering the deployment of lysosomes in the synapse to defend the tumor target cells from CTL attack. Their analyses also demonstrated that melanoma nodules in vivo adopt an unexpected configuration in which lysosomedense melanoma cells confront the T-cell-enriched microenvironment, highlighting the potential relevance of this molecular defense mechanism in the clinical context. See article

Oncogenetics OCC

Coordinator: Pr Rosine Guimbaud

Main collaborations:

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

STRATEGIC DIRECTIONS



The Oncogenetics OCC 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 OCC 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 OCC, 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, in search of genetic predisposition factors that may be responsible for an increased risk of breast cancer in men. This work has recently been submitted for publication. The second part of the project consists in analyzing the constitutional data of these patients using exomes, thanks to support from the Ligue Régionale contre le Cancer. Additional funding from the Ligue Nationale contre le Cancer has been obtained to pursue the project where AI will be used to combine these exome-based genetic data with patients' real-life data, e.g. exposure to various toxic substances, psycho-social data, etc. The objective is to establish a multifactorial MBC risk profile.

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



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 10year 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).

ONCOGERIATRICS & ENT PATHOLOGIES



Coordinators: Dr Loïc Mourey & Agnès Dupret-Bories There is currently no consensus on the management of patients with cancer of the upper aerodigestive tract over the age of 65. Since these patients may be frail, they are not always offered surgery. However, a single-center retrospective study of 188 patients suggests that surgery is the optimal treatment for most of them. <u>See article</u>

PEACE-1 RESULTS



Investigator: Dr Loïc Mourey

PEACE-1 (NCT01957436) is an international Phase III trial designed to assess the clinical benefit of the combination of abiraterone + prednisone, in addition to standard therapy (androgen suppression +/docetaxel) with or without radiotherapy, in patients with metastatic castration-sensitive prostate cancer (CSPC). Results published in 2022 support the combination of androgen suppression with docetaxel and abiraterone. This combination therapy improves overall survival and progression-free survival, with moderate side-effects, particularly hypertension. Dr Loïc Mourey presented the results of the elderly subgroup at ASCO GU 2023. <u>Read the article</u>

PRESIDENCY OF DIALOG



Since this year, Dr Loïc Mourey has co-chaired the DIALOG French Oncogeriatrics Research Intergroup with Pr Florence CANOUI-POITRINE (Epidemiologist, Hôpital Henri Mondor Créteil), whose accreditation by INCa has been renewed for five years. Its main objectives are to federate, facilitate and innovate to promote research in oncogeriatrics in France. More info

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

IMPALA: ASSESSING THE SEQUELAE OF CHILDHOOD RADIOTHERAPY



Coordinator: Pr Anne Laprie

IMPALA is a study launched in 2020 in collaboration with the Inserm ToNIC (Toulouse NeuroImaging Center) team. The initial results of this study, coordinated by Prof. Anne Laprie, were presented at the annual congresses of the Paediatric Radiation Oncology Society (PROS) and the International Society of Pediatric Oncology (SIOP). Based on data from 60 patients, we were able to identify changes in memory that were highly specific to radiotherapy, using both tests and multimodal imagery. In addition to the hippocampi, the caudate nucleus also appears to be affected. These results were reported in a scientific article published in 2023 (NCT04324450).

FINANCING BEACON2

Investigator: Dr Marion Gambart

BEACON1 is an international study coordinated by the University of Birmingham and designed to assess the benefits of combining an anti-VEGF monoclonal antibody with a standard chemotherapy regimen in children with relapsed or refractory neuroblastoma (NCT02308527). The letter of intent to continue this project (BEACON2) was accepted for PHRC-K funding in 2022.

CURALASE01 TO REDUCE CHEMOTHERAPY-INDUCED PAIN



Coordinator: Pr Marlène Pasquet

Now including 18 treatment centers in France, the CURALASE01 study launched in May 2021 aims to evaluate the administration modalities of an innovative treatment to relieve pain associated with chemo-induced mucositis in children: low-energy laser. It is funded by PHRC-K. Inclusion is still ongoing (NCT04596410).

INTERPEDIA SURVEY: PRELIMINARY RESULTS



Coordinator: Pr Marlène Pasquet

The aim of this INCa-funded project is to decipher the hematological phenotype of patients with the GATA2 mutation, using relevant new models to better assess the leukemic risk and the role of allogeneic transplantation. This project is the result of collaboration with the IRIT@CRCT team and the CRCT's IGAALD team. Initial work on a Franco-Belgian and British cohort was the subject of an publication accepted in Haematologica at the end of 2022, as well as communications, notably at the annual congress of the *European Hematology Association* (EHA). <u>Read the publication</u>

LAUNCH OF THE APACIS STUDY



Coordinator: Pr Marlène Pasquet

The main objective of this study is to evaluate changes in sensitivity to insulin, a hormone that acts on sugar in the body, as well as on other metabolic, motor and nutritional parameters in children with cancer, through the practice of moderate adapted physical activity or stretching. The adapted physical activity program is expected to produce better metabolic, motor and nutritional outcomes than the stretching program (NCT05383092).

Ear, Nose and Throat OCC

Coordinators: Pr Sébastien Vergez & Dr Anouchka Modesto

Main collaborations:

<u>Team T2i et the CRCT</u> (Coordinator: Pr Maha Ayyoub), <u>Team RNAreg</u> (Coordinator: Dr Stefania Millevoi) and <u>Laboratory CIRIMAT - UMR CNRS INPT UPS 5085</u> (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.

TWO GORTEC PUBLICATIONS



Investigators: Dr Anouchka Modesto

Two phase II trials under the aegis of GORTEC were published in 2022. One of them reported the first randomized trial comparing pembrolizumab and cetuximab in combination with radiotherapy in patients with advanced squamous cell carcinoma of the head and neck (see article). The other trial assessed the efficacy of afatinib-based maintenance therapy following post-operative radio-chemotherapy in squamous cell carcinoma of the head and neck (see article).

INDIVIDUALIZED VACCINATION: PRELIMINARY RESULTS

Investigator: Pr. Jean-Pierre Delord

The first non-viral-induced ENT cancer patient to benefit from the TG4050 individualized vaccine in Europe is an IUCT-Oncopole patient who was included in an early phase trial (NCT04183166). Preliminary data from the trial, which suggest that this non-invasive treatment is well tolerated by patients, were presented at the prestigious *American Society of Clinical Oncology* (ASCO) meeting in June 2022.

BIOMATERIALS: ANOTHER PROJECT!



Coordinator: Pr Agnès Dupret-Bories

In addition to the two projects awarded ANR funding in 2021 (BIOFISS and CongOs), Prof. Agnès Dupret-Bories launched a new biomaterial project in 2022. Supported by ITMO-Aviesan, the OSARM project aims to develop a hardening paste based on a new calcium phosphate cement loaded with polymer nanoparticles as drug reservoirs for customizable drug delivery for the treatment of osteosarcoma. Proof-of-concept was published in 2021. <u>View article</u>

A WORLD FIRST

Coordinators: Pr Agnès Dupret-Bories & Dr Benjamin Vairel For the first time in the world, the CIRIMAT/IUCT-Oncopole team has been able to offer a total nasal reconstruction using a biomaterial prosthesis. This was achieved in collaboration with Cerhum, a Belgian company specializing in bone reconstruction, which 3D-printed the prosthesis based on pre-treatment images. For the graft to be accepted, the porous biomaterial nose was cultured for two months on the patient's forearm. More info

FALCON STUDY RESULTS



Coordinator: Pr Agnès Dupret-Bories

The aim of this original project is to determine the individual professional and non-professional characteristics influencing the decision-making of physicians working in upper aerodigestive tract oncology. <u>See the article</u>

Sarcoma OCC

Coordinator: Dr Christine Chevreau

Main collaborations: Working closely with the <u>ONCOSARC</u> 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.

Launch of MEDISARC-RS

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

PHRC-I funding for HYPOSARC

Coordinator: Dr Justine Attal

HYPOSARC is a phase II trial evaluating the benefit of pre- or post-operative hypofractionated radiotherapy on wound healing in elderly or frail patients with limb or trunk soft tissue sarcoma. The first patients will be included in the trial in autumn 2023.

SPECIFICITY IN SURGERY



PERFOSARC analysis: results

Coordinator: Dr. Thomas Méresse Analysis of this database enabled the team to assess the reliability of pedicled perforator flaps in reconstructive surgery for limb and wall soft tissue sarcomas in adults. The results suggest the feasibility of this method, which should nevertheless be reserved for expert surgeons in referral centers. See article

EPOP-Sarcoma trial opens

Coordinator: Dr Dimitri Gangloff

The primary objective of this phase II study is to evaluate the value of surgical pre-habilitation in patients treated for limb soft tissue or bone sarcoma (NCT04515459).

TRANSLATIONAL RESEARCH



Continuation of PHRC K and PRTK 2018 studies

Coordinators: Dr Thibaud Valentin & Dr Frédéric Chibon Multicenter trial CHIC- STS 01 (PHRC-K)

Study evaluating peri-operative chemotherapy in softtissue sarcomas defined as high-risk by CINSARC, a molecular signature identified in 2010 by Dr Frédéric Chibon (NCT04307277).

MIRAS - SARRA (PRT-K 2018)

This multicenter translational cohort aims to characterize the clinical and biological features of rare soft tissue sarcoma (NCT04459234).

GSF-GETO Annual Meeting

The IUCT-Oncopole organized the annual Journées du Groupe Sarcome Français- Groupe d'Etude des Tumeurs Osseuses (GSF-GETO) from June 29 to July 1, 2022, in Toulouse. The event was a resounding success, with experts from all over France attending to discuss a wide range of clinical and scientific topics.

Senology OCC

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

Main collaborations:

DynACT team at the CRCT (Coordinator: Dr Salvatore Valitutti), <u>SIGNATHER team at the CRCT (</u>Coordinators: Pr Gilles Favre & Dr Olivier Sordet), <u>ONCOSARC team at the CRCT</u> (Coordinator: Dr Frédéric Chibon) & <u>«Cancer and Adipocyte Microenvironment»</u> 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 PARPi resistance

Coordinators: Pr Florence Dalenc, Dr Camille Franchet & Dr Jean-Sébastien Hoffmann

In June 2022, the IUCT-Oncopole launched a national project in collaboration with Artios Pharma Limited, a British biotech company pioneering the development of novel small-molecule therapeutics targeting the DNA damage response process, to understand the mechanisms of resistance to anti-PARP therapies in metastatic breast cancer patients with germline mutations of the BRCA1 and/or 2 genes. Entitled REPARP (REpair factor expression as biomarker of PARP inhibitor resistance), it seeks to understand the mechanisms of therapeutic resistance and improve survival in these patients. <u>Find out more about REPARP</u>

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.

A PUBLICATION IN NATURE!



Investigators: Pr Florence Dalenc, Dr Thomas Filleron & Amélie Lusque

Promoted by Unicancer, the SAFIR-02 BREAST trial (NCT03079011) is the first study coordinated by Prof. Fabrice André from the Institut Gustave Roussy to demonstrate the usefulness of the genomic sequencing of breast cancers in guiding patients towards personalized maintenance treatment. The Oncopole team made a major contribution to this trial, including 140 of the 1662 patients and randomizing 29 of the 238 patients (Pr Florence Dalenc, investigating physician), as well as performing the methodology and biostatistical analyses (Thomas Filleron, co-first author of the publication, and Amélie Lusque). See the article

Supportive Oncology Care OCC

Coordinators: Dr Nathalie Caunes-Hilary & Pr Virginie Woisard

Main collaborations:

IFERISS-CRESCO team (Coordinator: Pr Thierry Lang) and **BIOETHICS UMR1295 team** (Coordinator: Sandrine Andrieu)

EVALUATING NEW MODELS



Launch of TELEMSOS study

Coordinator: Dr Valérie Mauriès

Carried out in collaboration with the Inserm UMR1295 team (Pr Bettina Couderc) and the Groupe de Recherche et d'Analyse des Populations en Santé (GAP - Dr Sébastien Lamy), this project aims to study the contribution of telemedicine consultations, carried out by the Equipe Mobile Douleur Soins Palliatifs, in the follow-up of patients with chronic cancer. To find out more

Onco-sexology project wins APIRES award *Coordinator: Josiane Ménard*

This project, entitled «Acceptability and benefits of an onco-sexology course for laryngectomy patients and their spouses», is being carried out in collaboration with the Department of Surgery, and in particular Prof. Agnès Dupret-Bories. The aim is to improve their perception of intimate life.

FIGHT AGAINST PAIN



TEC ORL: publication of the protocol

Coordinator: Dr Antoine Boden

Funded by a PHRCI, this multicenter trial aims to evaluate the value of Qutenza in patients in remission from ENT cancer with sequelae of neuropathic pain (NCT04704453). Its protocol was published in 2022. See the article

Medical cannabis: where do we stand?

Coordinator: Dr Antoine Boden

The IUCT-Oncopole is a referral center for the ANSM's Medical Cannabis experiment (<u>Find out more</u>). Dr. Antoine Boden has published a review of the literature on the subject. <u>See the article</u>

Launch of DUNE study

Coordinator: Dr Antoine Boden

This real-life study was launched in March 2022 by the Centre Léon Bérard in Lyon. It seeks to evaluate the use of methadone for pain relief in patients inadequately relieved by other class 3 opioids (NCT05265442).

QUESTIONING ETHICS



Several scientific articles were published in 2022: on the paradoxes of silence in palliative care (Dr Marie Bourgoin - <u>see article</u>); on the flexibility of end-of-life legislation (Roxane Delpech and Pr Bettina Couderc -<u>see article</u>); and on the temporal challenges of deep and continuous sedation (Pr Bettina Couderc and Dr Nathalie Caunes-Hilary - <u>see article</u>).

The Comité de réflexion éthique is co-directed by Dr Nathalie Caunes-Hilary, Pr Bettina Couderc and Dr Guillaume Ducos. In 2022, it obtained international accreditation enabling it to assign an IRB number to non-RIPH research projects.

PRESERVING AUTONOMY



Coordinator: Pr Bettina Couderc

In 2022, the team launched a new project in collaboration with the Inserm UMR1295 team and the GAP group to establish the role of physicians in the adoption of written advance instructions in oncology. INCa, GSK and La Ligue contre le cancer are supporting this project with 237,000 euros in funding.

Thyroid and neuroendocrine tumors OCC

Coordinators: Pr Rosine Guimbaud & Pr Frédéric Courbon

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

NATIONAL AND INTERNATIONAL EXPERTISE



Several members of this OCC 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 OCC 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.

THYDOS PROJECT LAUNCHED



Coordinator: Dr Slimane Zerdoud

In collaboration with the Institut de Radioprotection et de Sûreté Nucléaire (IRSN) and the Commissariat à l'Energie Atomique et aux Energies Alternatives (CEA), a new machine has been developed to estimate in real time the dose of radioactivity received by an organ during medical irradiation. The next step is to validate the clinical use of this machine. Funding has been obtained in 2022 for this purpose. A subsequent project will verify the real benefit of this machine for the patient.

LAUNCH OF THE OXYTHYR PROJECT



Coordinator: Dr Lavinia Vija Racaru

Supported by the Ligue Régionale contre le Cancer, the OXYTHYR project aims to analyze metabolic cholesterol derivatives in the human thyroid, with a view to identifying markers of interest. The results are currently being analyzed and will shortly be published in scientific journals. Other projects are also in the pipeline, in collaboration with the INOV team at the CRCT.

LAUNCH OF THE PREPACLUNET PROJECT



Coordinator: Dr. Dierickx Lawrence

In collaboration with the DIAD team at the CRCT, the project seeks to demonstrate and validate the contribution of population pharmacokinetic (PK) methodology to the treatment of neuroendocrine tumors with a theranostic somatostatin analog (¹⁷⁷ Lu-Dotatate). The aim is to assess the correlation between treatment efficacy and toxicity and the PK profile, and to use this PK profile to personalize treatment.

EPILUNET REGISTER



Coordinator: Pr Rosine Guimbaud

EPILUNET is a national registry of Vectorized Internal Radiotherapy (VIRT) of endocrine tumors by ¹⁷⁷ Lu-Dotatate (Lutathera®), and is funded by the SFMN and the CNP of nuclear medicine. EPILUNET - for Epidemiology-Lutetium-NeuroEndocrine-Tumor - differs from a database or cohort in that it is exhaustive, unbiased and open-ended.

Urology OCC

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

Main collaborations:

<u>T2i team at the CRCT</u> (Coordinator: Pr Maha Ayyoub) and the Chemistry and Medicinal Biology for Oncology team at the IPBS (Leader: 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 Urology OCC team is an international pioneer in endoscopic monobloc bladder dissection techniques and is one of the few French teams performing thirdgeneration cryotherapy rescue techniques.

PARTICIPATION IN ONCO'LINK



The Urology OCC is taking part in the national Article 51 Onco'Link experiment launched at the IUCT-Oncopole at the end of 2022 for a period of two years. The aim is to strengthen collaboration between healthcare professionals and institutions in the coordinated management of patients treated with oral therapy. To find out more

PRELIMINARY RESULTS FROM BLAD-RAD01



Coordinator: Dr Jonathan Khalifa

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). Retrospective data were published in 2022 (See article).

SUGAR TRIAL LAUNCHED



Coordinator: Dr Guillaume Ploussard

SUGAR - *SUrGery With or Without dARolutamide in High-risk and/or Locally Advanced Prostate Cancer* is a phase II, multicenter, randomized, open-label, comparative trial designed to investigate the efficacy and safety of an androgen receptor antagonist (darolutamide) combined with surgery in patients with high-risk and/or locally advanced prostate cancer (NCT05826509).

PRESTO: RECRUITMENT BEGINS



Investigator: Dr Jonathan Khalifa

Coordinated by GETUG, PRESTO is a phase Ill randomized controlled trial evaluating the role of local ablative treatment of metastases in patients with hormonesensitive oligometastatic prostate cancer. The aim is to evaluate the efficacy of ablative radiotherapy (SBRT applied to all oligometastases) administered to all macroscopic tumor sites (metastases and prostate where appropriate), in patients with hormone-sensitive oligometastatic prostate cancer (NCTO4115007).

Department of Internal Medicine

Coordinator: Pr Odile Rauzy

Main collaborations:

METAML team at the CRCT (Coordinator: Dr Jean-Emmanuel Sarry), <u>EQUITY team</u> at the CERPOP (Coordinators: Dr Michelle Kelly-Irving & Dr Cyrille Delpierre), PEPSS team CIC 1436 (Coordinator: Dr Maryse Lapeyre-Mestre), <u>I2MC Inserm LIPSIPLAT team</u> (Leader: Pr Bernard Payrastre)

MISSIONS

The Department of Internal Medicine's expertise infections covers myelodysplastic syndromes, and in immunocompromised patients, rare immunohematological diseases (autoimmune cytopenias, genetic red-cell diseases, hereditary immune deficiencies, histiocytoses). It is a referral center for immunological manifestations associated with hemopathies and complications related to immunotherapy. It is involved in non-programmed care, in liaison with the departments of the IUCT-Oncopole, Toulouse University Hospital and the region.

MYELODYSPLASTIC SYNDROMES



Coordinators: Dr Thibault Comont & Pr Odile Rauzy

The Department of Internal Medicine is developing a new theme of real-life studies. Dr. Thibault Comont is coordinating the national evaluation registry for luspatercept in transfusion-dependent low-risk redcell myelodysplastic syndromes. The results of the preliminary studies are scheduled for 2023.

Vexas syndrome

Since 2020, a research focus at the Oncopole has been inflammatory manifestations associated with hemopathies, in particular Vexas syndrome. Dr. Thibault Comont is also a member of the group that created the French Vexas Registry (phenotype and molecular). An article published in 2022 based on data from this registry reported the efficacy and safety of azacitidine in 11 patients with VEXAS syndrome and myelodysplastic syndromes. <u>See article</u>

RARE IMMUNO-HEMATOLOGICAL DISEASES



The Department of Internal Medicine is one of four national reference centers for autoimmune cytopenias in adults (CeReCAI). Dr. Thibault Comont is a member of this network's scientific advisory board, and leads national studies including one on the use of splenectomy to treat immune thrombocytopenia (see article). The department is also a Center of Competence for sickle cell syndromes, thalassemic syndromes and other rare pathologies of the red blood cell and erythropoiesis, for hereditary immune deficiencies and for histiocytosis.

HEMOGLOBIN DISEASES



Coordinator: Dr Pierre Cougoul

The IUCT-Oncopole is an observatory center for the coexistence of sickle cell disease and oncohematological pathology (SICKLONE working group). In 2022, the team launched new clinical trials evaluating two molecules (the monoclonal antibody GBT21 and mitapivat), and is contributing to two AP-HP trials: the OSONE project (preventive strategy using highflow oxygen therapy) and the DREPARIC project (new transplant modalities for sickle-cell patients). The team is also collaborating on the Inserm IL PADRE study, which aims to investigate thrombo-inflammation in the aftermath of vaso-occlusive episodes. The team also contributed to the SISTER study, demonstrating the harmful effect of corticosteroid therapy in sickle cell patients, the results of which were published in Blood in 2022. See the article



Technical medical units



Department of Surgery

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

ESGO RE-ACCREDITATION



Coordinators: Pr Alejandra Martinez, Dr Gwénaël Ferron & Dr Laurence Gladieff

The surgery department has once again been accredited as a *European Training Center in Gynecological Oncology* by ESGO (*European Society of Gynecological Oncology*). The ESGO training program of excellence at Oncopole lasts between 2 and 3 years. It is based on a multidisciplinary approach and involves fellows in medical activities and, in partnership with the CRCT teams, particularly the T2i team, in research projects. The publication target is demanding.

RECONSTRUCTIVE SURGERY: STEPA



Coordinators: Pr Agnès Dupret-Bories, Dr Elodie Chantalat & Dr Mathieu Roumiguié

The team has obtained PHRCI funding for the STEPA project, whose ambition is to develop a new free flap for cervico-facial reconstruction: the STEPA external pudendal flap. This study builds on results previously achieved by the team: a <u>case report</u> published in 2019 and a <u>cadaveric study</u> in women published in 2022.

PAROLA PROJECT: WINNER OF A PHRC GRANT



Coordinator: Pr 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 Cance*r), 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).

TWO ONCO-GYNECOLOGY PUBLICATIONS ACCLAIMED



Coordinator: Pr Alejandra Martinez

In the summer of 2022, two articles from the oncogynecology team caught the interest of the editorial boards of two international journals:

• *Gynecologic Oncology*, which selected an article for its '*Editor's Choice*' in July. <u>Read the article</u>

• International Journal of Gynecological Cancer, which selected another article as its '*Publication Leader*' of the month. Bonus: an editorial by Jill Tseng and Robert E. Bristow (University of California, Irvine) and a podcast interview. <u>Read the article / Listen to the podcast</u>

RESULTS OF TWO GETTEC STUDIES



Coordinators: Pr Sébastien Vergez & Pr Agnès Dupret-Bories Under the aegis of the Groupe d'Etude des Tumeurs de la Tête et du Cou (GETTEC), Prof. Agnès Dupret-Bories coordinated a multicenter study evaluating salvage total glossectomy (TG) and total glossolaryngectomy (GLT), two surgical procedures that remain controversial because of their high morbidity. The aim was to describe oncological and functional outcomes after TG or TGL salvage. <u>See article</u>

Prof. Sébastien Vergez coordinated another study under the aegis of GETTEC that sought to define the indications for preventive tracheotomy in transoral robotic surgery (TORS) for head and neck cancers. Read the article

Medical Imaging Department

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

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

INTERNATIONAL REFERENCE CENTER

The department includes a radiology department, a radiosenology department and a nuclear medicine department, with a radiopharmacy unit and an inpatient sector for internal vectorized radiotherapy. The department's PET center is certified EARL 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). The IUCT-Oncopole Imaging Department is also a world PET validation center for General Electric Healthcare (GEHC).

1ST WORLDWIDE, THE FRUIT OF 20 YEARS OF COLLABORATION WITH GE HEALTHCARE

Coordinators: Pr Frédéric Courbon and Dr Olivier Caselles At the end of 2022, the IUCT-Oncopole will install Omni Legend[™], the new 100% digital PET-scanner platform co-designed with GEHC. This first worldwide is part of the tradition of collaboration between the two entities that began in 2006. Until March 2022, the IUCT-Oncopole was responsible for the physical and clinical evaluation of what was a non-commercial device intended solely for research purposes. The IUCT-Oncopole assessed the improvement in medical service rendered by the Omni Legend PET scanner compared with other PET scanners, thereby confirming the pertinence of the technological choices made. Collaboration is now ongoing in the fields of on-board artificial intelligence and detectors. VIRTUAL LESIONS TO TEST PET SCANS



Coordinators: Pr Frédéric Courbon & Dr Olivier Caselles As part of his PhD thesis under the supervision of Olivier Caselles, Quentin Maronnier has developed a hybrid methodology for simulating lesions in order to test the effectiveness of PET scanners. Based on the insertion of synthetic spheres into the raw data acquired prior to reconstruction, this methodology enables several scenarios to be simulated. <u>Read the article</u>

INCLUSIONS ONGOING FOR GENEBIOLUNET



Coordinator: Dr Lavinia Vija Racaru

The GENEBIOLUNET project, which is supported by GIRCI-SOHO, involves measuring the variability of molecular biomarkers that can characterize radionucleotide therapies (Lu-177 DOTATATE) in patients with metastatic midgut neuroendocrine tumors (NCT03667092).

Department of Medical Physics

Director: Dr Laure Vieillevigne Co-director: Grégory Hangard

Main collaborations: <u>RADOPT team</u> at the CRCT (Coordinator: Pr Elizabeth Moyal)

TWO NEW FACILITIES



The year 2022 heralded the arrival of two new machines that will be used with their first patients in early 2023. The first is the Halcyon 6 radiotherapy machine (Varian), which required the prior dismantling of another machine, as well as several weeks of validation and commissioning. The other machine is the Omni Legend PET/CT scanner developed by GE Healthcare in collaboration with the Department of Nuclear Medicine. The IUCT-Oncopole has been entrusted with evaluating the new AI-based reconstruction algorithm called Precision Deep Learning (PDL). The results of this work were presented at the European Association of Nuclear Medicine (EANM) 2022 and the Radiological Society of North America (RSNA) 2022 congresses. Scientific publications are also in preparation.

TWO NEW AWARDS



In July 2022, the department obtained Novalis Brainlab certification for a period of 4 years. This is an independent certification program for intra- and extra-cranial stereotactic radiotherapy based on international standards and publications from various radiation oncology institutions, including ASTRO and the IAEA. The end of 2022 was also marked by the recognition of IUCT-Oncopole's medical physics department as a PTW site, the world market leader in dosimetry solutions for radiotherapy, diagnostic imaging and metrology.

QUANTITATIVE ASSESSMENT OF PETS



Coordinator: Dr Olivier Caselles

As part of the installation of the Omni Legend PET/ CT scanner, Quentin Maronnier's thesis in medical physics focused on the development of an efficient methodology for inserting fictitious lesions to enable the quantitative evaluation of PET scanners based on different scenarios. The results have been published in the *European Journal of Nuclear Medicine and Molecular Imaging* (EJNNM) - *Physics*. Read the article

CORRECTIVE FACTORS FOR DOSIMETRY



Coordinator: Dr Laure Vieillevigne

Another thesis undertaken by Alexia Delbaere was the subject of a scientific publication in *Physics in Medicine and Biology* in 2022. This work focused on identifying corrective factors for the small-field dosimetry of new detection diodes. See the article

Radiotherapy Department

Coordinator: Pr Elizabeth Moyal

Main collaborations: Interconnections with the <u>RADOPT team</u> at the CRCT (Coordinator: Pr Elizabeth Moyal)

The radiotherapy department is highly involved in the INCa network RADIOTRANSNET, which focuses on preclinical radiotherapy research. Prof. Moyal is a member of the scientific committee.

RECOGNIZED EXCELLENCE



In the special edition of its magazine published in 2022, the *Organization of European Cancer Institutes* (OECI) hailed the excellence of the radiotherapy department, highlighting its quality approach and the integration of clinical and translational research. Testimony to this integration is the participation of several biology, imaging, and medical physics researchers in the department's projects, and in the interconnection with two INSERM teams, one at the CRCT (RADOPT) and the other on the Purpan site (ToNIC). The quality and structure of the department have also been recognized by the French Nuclear Safety Agency (ASN), which asked the team to give two lectures during the <u>seminar dedicated to the 2023 radiotherapy quality approach</u>.

HYPOSARC: PHRCI AWARDED

Coordinator: Dr Justine Attal

HYPOSARC is a phase II trial evaluating the benefit of pre- or post-operative hypofractionated radiotherapy on wound healing in elderly or frail patients with limb or trunk soft tissue sarcoma. The first patients will be included in the trial in summer 2023.

IA PARTNERSHIP WITH IRT ST-EXUPÉRY

Coordinator: Pr Elizabeth Moyal

In May 2022, the IUCT-Oncopole and the Institut de Recherche Technologique (IRT) Saint-Exupéry, an expert in AI for critical systems, established their collaboration by signing a partnership focused on AI. Several projects have already been launched:

• Predicting response to immunotherapy (PIRATE project co-directed by Pr Elizabeth Moyal and Ahmad Berjaoui)

 \cdot Using AI to predict MGMT promoter methylation (prognostic factor)

· Ability to differentiate molecular glioblastoma by Al

TUMOR-TREATING FIELDS (TTF)



Coordinator: Pr Elizabeth Moyal

In collaboration with the RADOPT team at the CRCT, the department is studying the mechanisms of resistance common to both radiotherapy and electric fields (TTF) to find new targets of interest to be inhibited in order to increase the efficacy of combining these two treatments. The team is using glioblastoma stem cells from the STEMRI trial (NCT01872221). A candidate protein has been identified and patented in partnership with Novocure. A clinical trial will be launched in 2023 to validate these results in patients. A prediction study will also be undertaken in collaboration with IRT-Saint-Exupéry. In addition, the IUCT-Oncopole is the first worldwide sponsor of the TRIDENT trial (NCT04471844), which aims to assess the benefits of adding TTF at the time of radiotherapy and throughout the STUPP protocol.

Medical Biological Oncology Laboratory (LBMO)

Coordinator: Pr Gilles Favre

Main collaborations:

Three teams at the CRCT share coordinators with the MBOL: Prof. Gilles Favre (<u>Team SIGNATHER</u>), Prof. Etienne Chatelut (<u>Team DIAD</u>), and Prof. Maha Ayyoub (<u>Team T2i</u>).

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)

OPTIMIZING URACILEMIA MEASUREMENT CONDITIONS

Coordinator: Dr Fabienne Thomas

Under the aegis of Unicancer's Groupe de Pharmacologie Clinique Oncologique (GPCO), a study was undertaken to refine pre-analytical recommendations for determining the uracil and dihydrouracil concentrations essential for reliable testing dihydropyrimidine dehydrogenase (DPD) deficiency. The authors concluded that caution is required when interpreting uracil concentrations if the time to centrifugation exceeds 1 hour at room temperature. This increases the risk of error in DPD status classification. <u>See the publication</u>

RESULTS OF THE PADA-1 STUDY



Investigators: Dr Anne Pradines & Pr Florence Dalenc Since 2018, the prospective biology unit has been one of the platforms involved in analyzing ESR1 mutations in circulating tumor DNA by digital PCR in the PADA-1 study piloted by Unicancer and the GINECO group (NCT03079011). The results of this study show for the first time that early detection of the ESR1 mutation in circulating DNA in patients treated with an aromatase inhibitor and an anti-CDK4/6 enables early adjustment of hormone therapy in favor of fulvestrant before clinical progression, thus significantly prolonging progressionfree life expectancy. 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 raise the question of the routine use of circulating DNA monitoring, which has already been incorporated into ongoing clinical trials. The findings were the subject of an article in The Lancet Oncology in 2022. See the article

MATADOR PROJECT LAUNCHED



Coordinator: Dr Christine Toulas

Male breast cancer is a rare pathology whose pathophysiology is poorly understood. Supported by La Ligue nationale contre le cancer, the MATADOR – Male breAsT cAncer preDisposition factOR project, headed by Dr Christine Toulas, aims to identify new predictive factors for this cancer. It is a collaborative project involving the Oncogenetics Laboratory and the EQUITY (UMR1295 – CERPOP) and REVA (Institut de Recherche en Informatique de Toulouse – IRIT) teams. To find out more

Oncohematology Laboratory

Coordinator: Pr Véronique De Mas

Main collaborations:

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

A WELL-KNOWN LABORATORY



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.

MOLECULAR/CYTOGENETIC PROFILES AND RESIDUAL DISEASE IN AML AND MYELODYSPLASTIC SYNDROMES



Two publications in 2022 by Pr Eric Delabesse showcased the laboratory's work in identifying the molecular and cytogenetic profiles of a) hyperleukocytic acute myeloblastic leukemias (AML) in *Blood Cancer Journal* (Read the article), and b) myelodysplasias with 11q deletions in *Blood Advances* (Read the article).

A study coordinated by Dr François Vergez highlights the prognostic impact of residual disease measured by flow cytometry in AML, with the development of a hybrid calculation method.

FAMILIAL AND GENETIC HEMOPATHIES

The laboratory regularly collaborates on projects involving familial and genetic hemopathies. In 2022, work on germline mutations of the *DDX41* gene carried out within the ALFA-FILO cooperative group led to a publication in Blood. <u>Read the article</u>

GENOMIC STUDIES IN MYELOMA



Several genomics projects coordinated by Pr Hervé Avet-Loiseau and Jill Corre on myeloma led to publications in 2022, including the evaluation of subclonal populations using a *single cell* approach (project funded by the Riney Foundation - See article published in *Journal of Clinical Oncology*), the study of the genomics of plasma cell leukemia (project funded by the IFM / See article published in Blood) and the preliminary results of the GAMER project - *Genomic Abnormalities of unexplained early relapse (funded by the Toulouse Cancer Santé Foundation*) published in Blood.

AI PROJECTS



The creation of the IRIT@IUCT-O team in 2021 has given rise to two projects in collaboration with the oncohematology laboratory. One of the projects, which is coordinated by Dr. Sarah Bertoli and Dr. David Simoncini, involves Dr. Jean-Baptiste Rieu digitizing diagnostic myelograms of acute myeloid leukemia (AML) (2,000 adult patients) and developing Al-based cell labeling tools to search for prognostic markers, in collaboration with the Hematology OCC. The other project, which is coordinated by Dr Marlène Pasquet, will characterize GATA2 patients on phenotypic, molecular and genetic criteria. To find out more

Pharmacy

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

Main collaborations: <u>DIAD team</u> at the CRCT (Coordinator: Pr Etienne Chatelut)

LEVERAGING ACCESS TO INNOVATION



Derogatory access: Innovative organization

Coordinators: Dr Camille Vinson and Dr Anais Grand Faced with the boom in requests for special access to medication that has not received market authorization, particularly in oncology, the IUCT-Oncopole pharmacy conceived an innovative protocol to manage these drugs following the overhaul of the system in July 2021. A dedicated team was deployed in 2022 to centralize all requests for access (early or compassionate), as well as collecting the data required to organize this special access and coordinate its provision. In addition, the IUCT-Oncopole the pharmacy has developed its own custom-bult software to manage this activity, in conjunction with an independent developer.

Article 51 concerning Expensive Molecules Coordinator: Dr Camille Vinson

This experiment concerns only five health establishments. Since 2021, the pharmacy has entirely coordinated the oncology part of the Article 51 Expensive Molecules experiment at national level. It is currently assessing the benefits of a more comprehensive approach to prescribing certain drugs. In conjunction with the DIM and DSI, the pharmacy has set up a system for collecting additional information on the context of the prescription, the indication for treatment and the effects of the treatment on patient care, for all anti-cancer prescriptions.

Onco'Link: Article 51 for oral therapies

Coordinators: Dr Jean Marie Canonge & Dr Charlotte Morel Launched at the end of 2022 at the IUCT-Oncopole, the Onco'Link experiment aims to strengthen city-hospital collaboration to improve the home management of oral therapies and their adverse effects, and to offer hospital pharmacy support to independent professionals. Ultimately, the aim is for the Ministry of Health to fund this activity, which has become essential for administering oral anticancer drugs.

SPECIFIC RESEARCH



Coordinator: Dr Florent Puisset

Many drugs, particularly oral anticancer agents, are available only in dry dosage forms, which are unsuitable for patients with swallowing disorders. Our pharmacy has long been involved in the preparation of oral suspensions of anticancer drugs, whenever published data allow. The limit to this activity is linked to all the research work required before being able to offer new galenic forms (validation of formulation. physico-chemical stability, and dose homogeneity). In 2022, work began to create the preparatory and control laboratory, thus enabling the pharmacy to conduct its own studies. Under the coordination of Dr Coralie Guillemot, this new unit will be responsible for developing and validating new formulations to extend the pharmacy's catalog of formulations and meet medical demand. Dr Pauline Claraz will be writing her doctoral thesis on the formulation of a vehicle for oral suspension, including rheological studies, physicochemical stability, and impact on bioavailability.

Pathology platform

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

Main collaborations: <u>NoLymIT team</u> at the CRCT (Coordinator: Pr Camille Laurent) & <u>DynAct team</u> 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).

FOCUS ON LYMPHOMAS



Creation of a national lymph node inventory

Coordinators: Pr Camille Laurent & Pr Pierre Brousset This is a national inventory of lymph nodes collected either by core biopsy (CNB) or by surgical excision, in order to compare their diagnostic performance for lymphoma in routine pathologic practice. A total of 32,285 cases from the Lymphopath network have been reviewed. CNB proved less conclusive than surgical excision, underlining the need for systematic expert review of suspected lymphoma. See article

Launch of the DIAL project

Coordinator: Pr Pierre Brousset

DIAL - Diagnostic Assistance of Lymphoma benefits from the complementary expertise of seven academic research teams from French centers (including IUCT-Oncopole and CRCT), LABEX TOUCAN, Institut Carnot CALYM and an industrial partner (Roche). Focusing on diffuse large-cell B lymphomas and peripheral T lymphomas, it aims to develop a diagnostic assistance platform based on machine learning algorithms.

Resistance to Car-T cell treatment

Coordinators: Pr Camille Laurent & Dr Charlotte Syrykh Prof. Camille Laurent and Dr. Charlotte Syrykh have found that genetic remodeling is a possible explanation for the resistance of lymphomas to Car-T cell treatment. Acquired mutations in the PI3K and KRAS pathways have also been demonstrated to be potential targets for complementary therapies to overcome resistance to Car-T cell treatment. <u>Read the article</u>

Biological Resource Center (BRC)

Coordinator: Pr Anne Gomez-Mascard

ON THE ROAD TO NEW CERTIFICATION

The BRC has held dual ISO 9001:V2015 and NF-S-96 900 certification since 2020, enabling it to respond to calls of international scope, and through positive participation – since this was mentioned as a strong point of the site – in the OECI certification process (obtained in June 2020), as part of the IUCT-Oncopole Comprehensive Cancer Center label. The BRC also plans to obtain ISO 20387 certification in 2023, one of whose requirements is to function according to the principle of impartiality. Indeed, its organization implies the absence of bias and the making of decisions in an objective, fair and equitable manner. The management, the scientific advisory board and all staff act with impartiality in the missions entrusted to them.

NEW COLLECTIONS



The BRC possesses 26 collections, 12 of which originate from in-house procedures (+ a series of samples) and 12 other hosted collections, for a total of 230,000 samples (tumor and non-tumor). In 2022, four new collections were added:

• IMMUNODIG MSI cohort (immunotherapy tolerance of digestive tract tumors) (<u>HDH-F20210315164546</u>)

INSPIRE: murine collection of biomarkers of biological aging (NCT04224038)

- · Collection of hematological malignancies
- Canine osteosarcoma collection

SIGNIFICANT INCREASE IN ACTIVITY



In 2022, the BRC witnessed a considerable increase in the number of collections received and stored. The volume of preparation and provision activity also increased. A total of 56,626 new samples were received, representing more than 208,000 stored frozen samples and 26,000 paraffin-embedded blocks. Preparation activities increased by 73% compared with 2021, with 29,000 samples/derived products (white slides, chips, slide scans, DNA and RNA extraction, paraffin-embedded blocks, TMA). The number of samples/derived products made available rose by 92% to 18,922. Overall, the BRC was involved in 85 projects, including 48 research projects. Since 2021, the team has been reinforced by an ARC dedicated to projectspecific clinical data research.

SETTING UP AN 'ANIMAL' FACILITY



To meet the needs of CRCT researchers, an 'animal' pathology facility has been created. Several machines have been acquired for this purpose (stainer, dehydrator), and staff dedicated to this activity have been trained.



Resuscitation and Continuing Care Unit

Coordinator: Dr Guillaume Ducos

Main collaborations:

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

PROSPECTIVE MULTICENTER STUDIES

PIC and DéPOH projects

Investigator: Dr. Muriel Picard The IUCT-Oncopole ICU is participating in two randomized multicenter studies - DéPOH (coordinator Dr Djamel Mokart, sponsor IPC Marseille, <u>2015-022</u>) and PIC (coordinator Dr Virginie Lemiale, sponsor AP-HP, <u>P150961</u>) - 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. Further plans to participate in multicenter studies within the Grrr-OH are underway.

VIROH STUDY

Sponsor: CHU Toulouse Coordinator: Dr Muriel Picard - local investigators: Dr Amazigh Aguersif, Dr Sihem Bouharaoua

This nationwide multicenter retrospective study (11 Grrr-OH centers) is investigating thoracic CT features and their association with outcome in patients with hematologic malignancies admitted to the ICU from 2008 to 2018 for acute respiratory failure with respiratory viral documentation. *Orthomyxovirus* infections were found to cause bronchoalveolar syndrome more frequently than *Paramyxovirus* infections. Alveolar syndrome proved to be a risk factor for invasive mechanical ventilation, unlike bronchial syndrome. Overall lesion intensity was associated with the use of invasive mechanical ventilation and death in the ICU. Article to be published in *European Respiratory journal*.

MED-HEM STUDY



Sponsor: CHU Toulouse Coordinator: Dr Muriel Picard

National multicenter retrospective study (Grrr-OH) on thoracic CT characteristics and their association with the outcome of patients with a diagnosis of hematologic malignancy admitted to the ICU from 2014 to 2021 for mediastinal mass syndrome. Data collection in progress (Camille Alric, Julie Avet-Loiseau).

SOCIÉTÉ FRANCOPHONE DE GREFFE DE MOELLE ET DE THÉRAPIE CELLULAIRE WORKSHOPS



The IUCT-O ICU participated in the SFGM-TC Harmonization Workshops in September 2021 on complications after CAR-T cell treatment. This led to a publication in the journal Bulletin du Cancer that detailed recommendations for the management of neurotoxicity syndrome, cytokine release syndrome and infectious complications.

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

Patient inclusions in ER-One

Oncopole investigator: Dr Régis Fuzier

This randomized, non-inferiority, multicenter, doubleblind clinical trial is being conducted by the Institut de Cancérologie de Lorraine. Awarded a PHRC-K grant, its aim is to evaluate the effect of erector spinal block (ESP) versus paravertebral block (BPV) on acute pain after breast surgery (<u>NCT04827030</u>). Inclusion began in 2022.

ANTICIPATING RISKS



Launch of the ERION study

Coordinators: Dr Delphine Vallot & Dr Régis Fuzier The Emission Rayonnement Ionisant (ERION) project is a single-center retrospective study designed to assess the impact of training on the emission of ionizing radiation by image intensifiers during the installation of catheter holders. The results will be published in 2023.

SFAR Recommendations & Human Factors Coordinator: Dr Régis Fuzier

In collaboration with the Société Française d'Anesthésie et de Réanimation (SFAR), work has been carried out to draw up recommendations for professional practice, taking into account the importance of human factors in critical situations. The results of this work will be published in 2023.

Partnership with IRT St-Exupéry

As part of the partnership signed in 2022 with the Institut de Recherche Technologique (IRT) Saint Exupéry, a project has been launched to design a tool to assist in making anticipatory therapeutic decisions, based on predictive indexes of the occurrence of intraoperative arterial hypotension. The algorithm has been validated and the data is currently being analyzed. The IUCT-Oncopole is accredited by:





Publication Coordinators: Pr Jean-Pierre Delord, Pr Gilles Favre, Jean-François Lefebvre, Claire Genéty Editorial board: Fleur de Lempdes, Anne-Laure Fize, Lise Baylet, Élise Baylocq Conception and realisation: Clémence de Bona



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