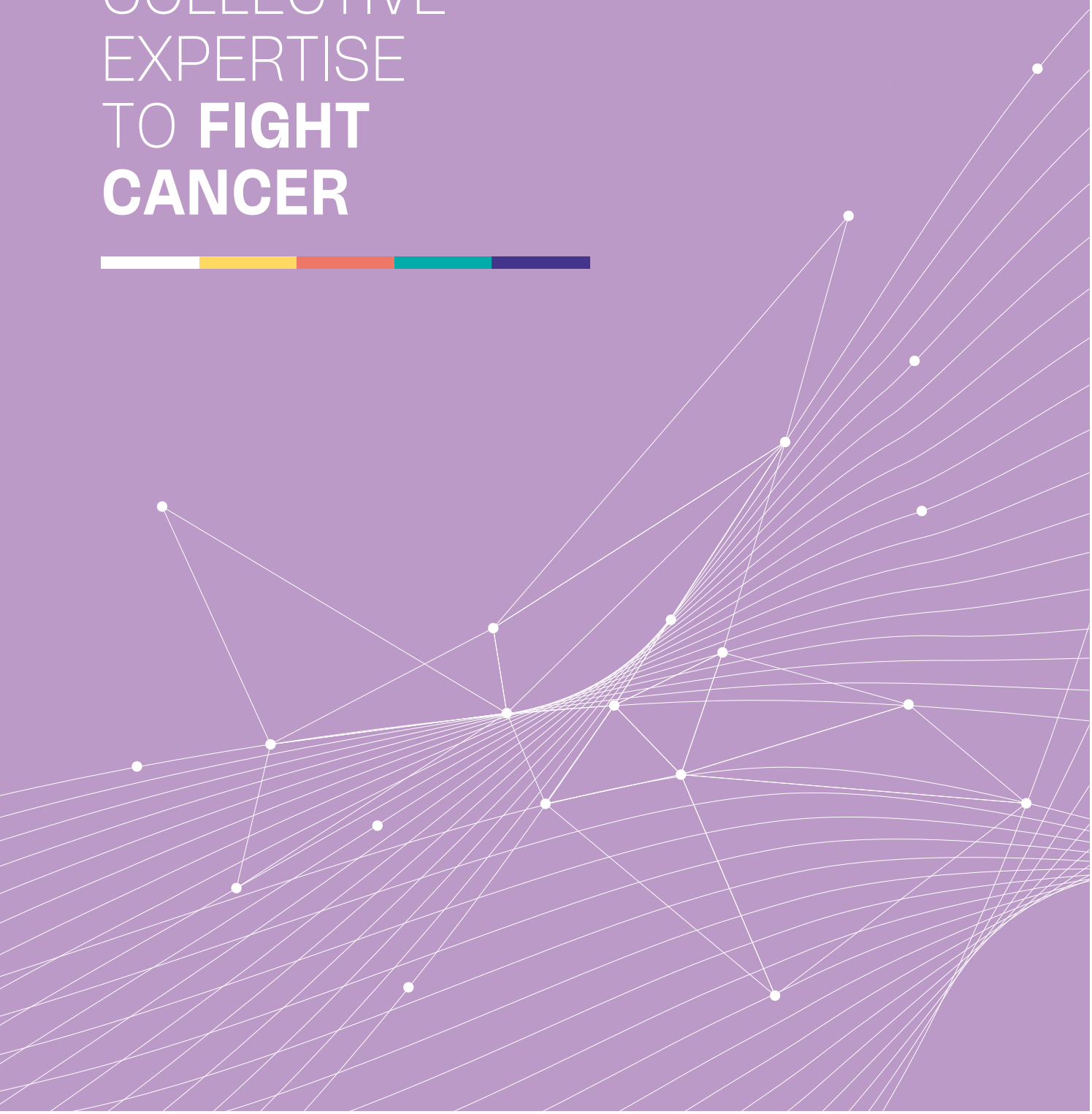
FOCUS RESEARCH
2023

INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
Oncopole

COLLECTIVE EXPERTISE TO **FIGHT CANCER**



CONTENTS

Impact & achievements

Key figures 2023

RESEARCH

LESS THAN

6

MONTHS

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

147

RESEARCHERS

126

ENGINEERS AND RESEARCH TECHNICIANS

68

INTERNATIONAL PUBLICATIONS

with an impact factor **> 20**

26

NATIONALITIES

among the different researchers

1

LABORATORY OF EXCELLENCE: TOUCAN

20

RESEARCH TEAMS

8

TECHNICAL RESEARCH PLATFORMS

1

ERC GRANT: ATTACK

European Research Council
Established by the European Commission

CLINICAL TRIALS

369

CLINICAL TRIALS

opened for inclusions in 2023

43%

EARLY PHASE TRIALS

1,563

NEW PATIENTS

included in 2023

2x

as many clinical trials — a figure that has doubled since the creation of the IUCT-Oncopole **10 YEARS AGO**

13,6% of the active file of patients included in a clinical trial in 2023

INCLUSIONS

41%

SPONSORED BY THE IUCT-ONCOPOLE

39%

SPONSORED BY ACADEMIA

20%

SPONSORED BY INDUSTRY

DETAILS PER TEAM

Toulouse Cancer Research Center (CRCT)

CRCT MICROPANC team

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 | Patient-derived experimental models | Targeted nanotherapies | (polysome) RNAseq & bioinformatics | Matrisome | Multiplexed tissue imaging

PROJETS

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

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

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

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

FOCUS 2023

Research coordinated by Dr Corinne Bousquet
Focuses its research on the discovery of specific roles for cancer-associated fibroblasts in pancreatic cancer, and of underlying dialogs with their cellular neighborhood, including through development of in vivo immunocompetent murine models (Acta Cir Bras, doi: 10.1590/acb382823); in 2023, the team participated in the identification of ion channels (Gut, doi:10.1136/gutjnl-2021-326610) and of trogocytosis events (BioRxiv, doi:10.1101/2023.09.15.557802), as novel molecular exchange routes that trigger cancer cell agressiveness, or of a specific subset of CAFs involved in suppression of antitumor immunity. Read the article

→ Discover the team's publications

CRCT RADOPT team

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 – More info
- **Effects of Pesticides in carcinogenesis and resistance to radiotherapy and chemotherapy in glioblastoma** – Coordinator: Dr Augustin Le Naour – More info
- **Optimizing the determination of absorbed dose in external radiotherapy** – Coordinator: Dr Laure Vieillevigne & Dr Alexia Delbaere – More info
  - Project 1: Determination of a code of practice for determining the absorbed dose in heterogeneous media from experimental measurements of photon beams
  - Project 2: Development of a computational radiobiology platform modeling and assessing the physical and biological effects of combined therapies
- **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 2023

Research on TTFields, a new therapeutic modality for glioblastoma

Only a few therapeutic advances have been made in the treatment of glioblastoma (GBM) over the past decades, but Tumor Treating Fields (TTFields) have achieved improved outcomes in clinical trials. TTFields are now a part of the first-line clinical treatment for newly diagnosed GBM and malignant pleural mesothelioma; additional clinical trials are recruiting or ongoing in multiple other solid tumor types (https://novocuretrials.com/). TTFields are a noninvasive, physical, local therapy that relies on the delivery of alternating electrical fields with low intensity and intermediate frequency. They target cancer cells by disturbing the localization and polymerization of polar molecules, thus altering their functions and a multitude of biological processes. In fact, they mainly disrupt cancer cell mitosis, but also perturb cell invasion and migration, autophagy, the DNA damage response and repair, the immune response and angiogenesis. Interestingly, due to their multimechanistic actions, TTFields have been described as acting additively or synergistically with other cancer treatments. However, not all patients react in the same way to treatments, including electric fields, and it is important to better study factors of sensitivity or resistance to TTFields.
Toulouse is a leader in France on TTFields research which is coordinated by Pr Elizabeth Moyal. This topic is investigated by Dr Valérie Gouazé-Andersson and Dr Pauline Deshors through preclinical work in the RADOPT laboratory and the Radiotherapy Department of the IUCT-Oncopole, both of which led by Pr Elizabeth Moyal. Notably, IUCT-Oncopole is one of the centers involved in the worldwide TRIDENT Phase III Clinical Trial with Pr Elizabeth Moyal as the Principal Investigator. This clinical trial is evaluating the safety and efficacy of TTFields paired with radiation therapy and temozolomide in newly diagnosed GBM patients.

Discover the team's publications

CRCT SIGNATHER team

Cellular signaling, oncogenesis and therapeutics

Coordinators: Pr Gilles Favre and Dr Olivier Sordet

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

PROJETS

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

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

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

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

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

FOCUS 2023

Development of a technique to identify RHO GTPase inhibitors
The SIGNATHER team has identified a new treatment able to prevent the development of resistances to targeted therapies in lung cancer, one of the greatest current public health challenges. They discovered that tumor cells stop dividing within the first few hours of treatment and revert to a state resembling that of normal alveolar lung cells. Although most cells end up dying, a small proportion can adapt and progressively regain proliferative capacities, ultimately causing relapse. The transition between the different states requires an enzyme called farnesyltransferase, and pharmacological inhibition of this enzyme hampers the adaptation of tumor cells to treatment, leading to their death. Combinations of targeted therapies and farnesyltransferase inhibitors are currently in early-phase clinical trials and represent a real hope for reducing relapse in patients. To find out more

Discover the team's publications

CRCT R'n Blood team

RNA biology in hematological tumors

Coordinators: Dr Stéphane Pyronnet & Dr Fabienne Meggetto

This team is part of the Labex TOUCAN.

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

PROJETS

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

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

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

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

FOCUS 2023

L'Oréal-UNESCO Foundation Award
Stéphane Pyronnet and the Group's bioinformaticians took part in the launch of the first «k-mer days» workshop (June 23-24, Sète, France), aimed at bringing together multidisciplinary scientists to develop innovative pipelines dedicated to the exploration of next-generation sequencing data.
The CircOma project led by Fabienne Meggetto's group in collaboration with the Bioinformatics and Biomarkers team (INSERM U1183, Montpellier) and the Hematology Laboratory of the Institut Gustave Roussy (Villejuif) is a winner of the PRTK-2023 program (DGOS and INCA). It aims to decipher the role of circular RNAs in the pathogenesis and therapy resistance of ALK-positive anaplastic large-cell lymphoma. Read more

Discover the team's publications

CRCT SigDYN team

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 – More info

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

· **Functions and regulation of PI3K isoforms in pathophysiology** – Coordinators: Dr Benoît Thibault – More info

FOCUS 2023

CLUSTER : an ovarian clinical trial ancillary study – start of enrolment in 2023
The morphology and cellular composition of tumor cell clusters found in ascites from patients with High-grade serous ovarian cancer (HGSOC) determine the mechanical constraints of these structures, which are translated into intracellular signals (mechanotransduction). Our team has started a CLUSTER ancillary study linked to the PLATINOV clinical trial (Dr Ferron, IUCT-O), which will enable us to prospectively analyze their diagnostic and predictive values. This project involves the complementary skills of Dr Céline Basset (Basset C Ann Pathol 2023; Basset C Ann Pathol 2023), Dr Benoit Thibault (Thibault B Cancers 2023) stably recruited as Researcher in 2022, Dr Julie Guillermet-Guibert (Schmitter 2023, Ben Meriem 2023) and benefits from the last recruitment of Dr Romina D'Angelo, a specialist in 3D imaging (CNRS LLPI 2023 competition laureate image).

Discover the team's publications

- A microfluidic mechano-chemostat for tissues and organisms reveals that confined growth is accompanied with increased macromolecular crowding – Ben Meriem Z et al, Lab Chip. 2023 Oct 10
- Transducing compressive forces into cellular outputs in cancer and beyond – Schmitter C et al, Life Sci Alliance. 2023 Jun 26
- Targeting Class I-II-III PI3Ks in Cancer Therapy: Recent Advances in Tumor Biology and Preclinical Research – Thibault B et al, Cancers (Basel). 2023 Jan 27
- Mechanistic target of rapamycin (mTOR) regulates self-sustained quiescence, tumor indolence, and late clinical metastasis in a Beclin-1-dependent manner – Nicco C et al, Cell Cycle. 2023 Mar
- Serous fluid cytopathology : International system: Ancillary studies for serous fluids and special considerations for peritoneal washings – Basset C et al, Ann Pathol. 2023 Nov
- Serous fluid cytopathology: International system – Basset C et al, Ann Pathol. 2023 Mar
- Ephrin-B1 regulates the adult diastolic function through a late postnatal maturation of cardiomyocyte surface crests – Karsenty C t al, Elife. 2023 Jan 17

CRCT NetB(IO)² team

Network Biology and PI3K isoforms

Coordinator: Dr Vera Pancaldi

Specific themes
Computational biology | Single-cell and spatial transcriptomics | Genome architecture | System biology | Immune system | Tumour microenvironment heterogeneity

PROJETS

· **Targeting the tumour microenvironment: blocking tumour-associated macrophages and activating γδ T lymphocytes** – Coordinator: Dr Mary Poupot – More info

· **Multiscale dynamical modelling of cellular interactions in the tumour microenvironment** – Coordinator: Dr Nina Verstraete – More info

· **Spatial organisation of the tumour microenvironment and multi-omics approaches** – Coordinator: Dr Vera Pancaldi – More info

· **Epigenomics and chromatin networks** – Coordinator: Dr Vera Pancaldi – 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 2023

Studying 3D DNA in the nucleus

One area of our work involves modelling tumours as systems in which cancer cells interact with several other cell types.
In 2023, we published our first model of the interaction between monocytes and cancer cells. Many cancers can be treated by invigorating lymphocytes, whose role is to defend our body against attack, with specific drugs. Unfortunately, only a minority of patients and only certain types of cancer can be treated in this way. One of the reasons is that, in some cases, cancer cells are able to corrupt other types of immune cells to protect them and prevent the infiltration of anti-cancer lymphocytes into the tumour tissue. The simple act of culturing cancer cells with monocytes (a type of cell present in the blood) transforms the latter into so-called «nurse» cells that protect the cancer cells from death in culture.
With the aim of gaining a better understanding of how these cells form, so that one day their formation could be in patients, we used a numerical model that represents cells as agents with specific behaviours to simulate their interactions in a culture dish, as if it were a video game. After checking that the simulation behaved like reality in a few situations, we were able to gain a better understanding of the important processes that take place leading to the formation of cancer-protective cells. We hope that in future our models will be able to make patient-specific predictions.

Discover the team's publications

CRCT NoLymIT team

New immunotherapies for lymphoma

Person in charge: Pr Camille Laurent

This team is part of the Labex TOUCAN and Institut CARNOT CALYM

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

Our work focuses on the innate and adaptive immune response in lymphoma with a special mention on the study of Tγδ lymphocytes and mechanisms of regulation of immune checkpoint expression.
Recently, we have introduced Single Cell RNAseq techniques includint spatial transcriptomic analyses and developed bionformatic tools allowing us to explore the functional status and maturation/differentiation stage of cytotoxic effectors at the single cell scale in samples lymph nodes or blood of patients with lymphoma.
Privileged access to different cohorts of lymphoma patients has also allowed us to identify biomarkers of response in lymphomas and the establishment of a screening platform in 3D models from patient samples lymphomas.

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 : link 1 | link 2 | link 3 | link 4

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

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

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

· **Decipher immune-escape mechanisms and resistance by multiomic approaches in lymphoma** – More info

FOCUS 2023

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 Eotvos 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

The NoLymiT team is principal investigator of the European THERAVLINFO project
THERAVLINFO is an advance in the biomedical translation of preclinical lymphoma knowledge and models generated in IMLINFO (EFA 281/16), in order to improve the survival and quality of life of patients with hematological cancer.
OBJECTIVE: To determine the effectiveness of new immunotherapy treatments through the creation of a NHL tumour bank associated with a 3D culture platform.
The project is part of axis 1 of the POCTEFA programme: Boosting innovation and competitiveness
To find out more

→ Discover the team's publications

CRCT METAML team

Metabolism and therapeutic resistance in acute myeloid leukemia

Coordinator: Dr Jean-Emmanuel Sarry

This team is part of the Labex TOUCAN.

Specific themes
Acute myeloid 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

FOCUS 2023

The aim of our team is to identify the mechanisms involved in the progression of acute myeloid leukaemia, as well as in the establishment of residual disease after treatment, which is a key factor in relapse. This year, we identified a new prognostic marker (CD36) and a metabolic vulnerability (ferroptosis) specific to FLT3 inhibitors, and demonstrated the involvement of autophagy in resistance to ruxolitinib. Our work also explores the importance of host autophagy, dormancy, epigenetic modifications and certain key players in RNA splicing (PTBP1) in this pathology.

→ Discover the team's publications

CRCT RNAreg team

RNA binding proteins and genotoxic stress

Coordinator: Dr Stefania Millevoi

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

PROJETS

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

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

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

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

FOCUS 2023

The RNAreg team, created by INSERM in 2021, brings together experts in the fields of protein synthesis (S. Millevoi and A. Cammas), autophagy (E. Espinos, S. Manenti), as well as clinicians (S. Vergez) around a central theme that aims to explore the biology of RNA in HNSCC cancer in response to genotoxic stress. The work of CRCT's RNAreg team in 2023 was leveraged by two collaborative articles: a database article in collaboration with E. Dassi (CIBIO, Trento, Italy) aimed at exploring RNA mechanisms modulating cancer gene expression in order to exploit them as potential therapeutic targets (Bourdon (2023) NAR), and an article resulting from synergy with C. Joffre's group at CRCT, highlighting the contribution of autophagy targeting to the sensitization of myeloproliferative neoplasms to therapies targeting the JAK signaling pathway (ruxolitinib) (Courdy (2023) Blood Cancer J). We have also initiated discussions on the use of organoids (PDO) to study ORL cancers, via the creation of a working group involving our team, Prof. Sébastien Vergez, the IUCTO ORL department, and the ORGAPRED platform in Caen.

Discover the team's publications

CRCT ImPact team

Therapeutic innovation in pancreatic cancer

Coordinator: Dr Pierre Cordelier

Specific themes
Pancreatic cancer | Oncogenesis | Resistance | Innovative therapies | Regulation of gene expression | Protein-protein interaction | Intracellular antibodies | Oncolytic viruses | Gene therapy | Immunotherapy | Interdisciplinarity

PROJETS

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

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

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

FOCUS 2023

Pancreatic tumors are notorious for their resistance to chemotherapy, which only extends patient survival from weeks to months. In this context, the ImPACT team has been investigating the therapeutic potential of gene therapy to help sensitize pancreatic tumors to gemcitabine. We previously identified that the expression of deoxycytidine kinase (DCK) and uridine monophosphate kinase (UMK) sensitizes pancreatic tumor cells to chemotherapy. In parallel, we found that restoring the expression of somatostatin receptor 2 (SSTR2) inhibits the proliferation and dissemination of cancer cells and cooperates with gemcitabine to inhibit tumor growth.
In this paper (PMID: 37063483), we report the preclinical investigations that laid the groundwork for phase I and II clinical trials in patients. In greater detail, we describe the development of the CYL-02 non-viral gene therapy product, which comprises a DNA plasmid encoding the three aforementioned genes. The expression of these genes is targeted to tumor cells and complexed with a polyethyleneimine non-viral vector. Preclinical toxicology, bio-distribution, and therapeutic activity studies of CYL-02 were performed in two rodent models of pancreatic cancer. These studies demonstrated that CYL-02 is safe, does not increase gemcitabine toxicity, is rapidly cleared from the blood following intravenous administration, and is sequestered in tumors following intra-tumoral injection. CYL-02 was validated during functional studies, as it drives the expression of therapeutic genes in cancer cells and strongly sensitizes tumor cells to gemcitabine, both in vitro and in vivo, resulting in significant inhibition of tumor cell dissemination. This study was instrumental in defining the dose and identifying safety markers for the subsequent use of CYL-02 in patients with advanced pancreatic cancer. It demonstrates that rigorous and thorough preclinical investigations are informative for the clinical transfer of gene therapies against this disease (PMID: 37063483).

Discover the team's publications

CRCT DIAD team

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

· **Oral therapies: Adapting oral anticancer drug dosages for patients unable to swallow**– Coordinators: Coordinators: Dr Cécile Arellano & Dr Florent Puisset – More info

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

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

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

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

· **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

· **Toward a better screening of DPD deficiency**– Coordinator: Dr Fabienne Thomas – More info PMID 36926988 PMID 36104927

FOCUS 2023

Multigene Panel Sequencing Identifies a Novel Germline Mutation Profile in Male Breast Cancer Patients

Coordinator: Ayman Al Saati
Male Breast Cancer (MBC) is a rare disease whose pathophysiology is poorly understood. The risk factor clearly identified to date is the presence of a germline mutation in the BRCA2, BRCA1 and PALB2 predisposition genes. However, in over 70% of cases, no mutation is identified. To identify new genes that could predispose to male breast cancer, we compared the genetic profiles of a cohort of 85 MBC patients with a cancer-free male control population, analyzing a panel of 585 genes involved in oncology. This comparative study enabled us to highlight the preferential presence, in the MBC cohort compared with the control population, of mutations in genes involved in DNA repair, genomic stability and other cellular functions.

→ Discover the team's publications

DETAILS PER ORGAN

Coordination Committee (OCC)

Gynecology OCC

Coordinator: Dr Laurence Gladieff

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

RARE TUMORS

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

TROPHAMET trial
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 diseases 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 lombo-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 standard chemotherapy with dostarlimab alone 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 paclitaxel-carboplatin 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 cytoreductive surgery (NCT05183984).

SUPPORTIVE ONCOLOGY CARE

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 (NCT03956498). 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:
NoLymIT team at the CRCT (Coordinator: Pr Camille Laurent), GENIM team at the CRCT (Coordinators: Pr Hervé Avet-Loiseau & Dr Ludovic Martinet), IGAALD team at the CRCT (Coordinator: Pr Eric Delabesse) and METAML team at the CRCT (Coordinator: Dr Jean-Emmanuel Sarry)

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 article). The second showed that these anomalies are present from the moment of diagnosis and often missed on mass analysis (see article).

RESISTANCE TO CAR-T CELLS

CLL : Prognostic value of IGLV3-21R11 mutation
In collaboration with IDIBAPS institute (Pr Elias Campo and Dr Ferran Nadeu, Spain), Dr Charlotte Syrykh developped a multiplex PCR assay to easily identify the IGLV3-21R110 mutation in a large cohort of CLL patients. They confirmed that IGLV3-21R110 mutation defines a subset of CLL with an intermediate epigenetic profile and agressive clinical course. They also found new associations between IGLV3-21R110 and other CLL driver alterations. (See article)

High-risk DLBCL : Alycante
Pr Camille LAurent coordinated the biological study of the LYSA ALYCANT trial, showing that Axi-cel as a second-line treatment achieved high response rates and durable remissions in high-risk DLBCL R/R patients with poor prognostic features. (See article)

Contributions to the new ICC classification
Pr Camille Laurent and Pr Pierre Brousset have contributed to the new International Consensus Classification of myeloid and lymphoid neoplasms, refining definition, recommended studies and criteria for the diagnosis of follicular lymphoma/marginal zone lymphoma (see article https://pubmed.ncbi.nlm.nih.gov/36394631/) and Hodgkin lymphomas. (See article)

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
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).

LAUNCH OF THE THEMIS STUDY

Coordinator: Pr Loïc Ysebaert
Since 2006, Toulouse has pioneered studies aiming at improving patients tolerance and compliance through telephone monitoring (Assistance aux Malades Ambulatoires, AMA). AMA nurses now have hundreds of patients in follow-up, but lack a clear demonstration of economic impact. The study THérapies ciblées et Evaluation Médico-économique d'un programme Infirmier de Suivi (THEMIS) has been launched in 2023, will be recruiting 450 CLL patients under oral therapy, and will randomize AMA or not to evaluate as a primary endpoint whether it is cost-effective. If this study is positive, as it is funded by the government through a PRME grant, will be used in other French centers to promote AMA for their own population of patients.

Neuro-oncology OCC

Coordinators: Pr Elizabeth Moyal & Dr Delphine Larrieu-Ciron

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

TRIDENT TRIAL

In the fight against glioblastoma, it is essential to increase the efficacy of standard treatments such as radiotherapy and chemotherapy. To this end, the **TRIDENT trial** aims to compare the addition of electric fields (TTFields) at the start of radiotherapy and chemotherapy with the current treatment integrating electric field therapy in the adjuvant phase after radio-chemotherapy. The world's N°1 center of inclusion in this clinical trial - 48 patients

STEMRI TRIAL

Magnetic resonance spectroscopy imaging can define tumor areas enriched in glioblastoma stem-like cells

A 100% Toulouse team composed of radiotherapists from the Oncopole, neurosurgeons from the Toulouse University Hospital, and the National Institute of Health and Medical Research (INSERM) researchers has just demonstrated the relevance of a new MRI technique to locate foci of aggressive tumor cells to improve the treatment of glioblastomas. This research has been published in the prestigious international journal Science Advances. (Read the article)

AI PARTNERSHIP

Coordinator: Pr Elizabeth Moyal

One year after signing their partnership agreement focusing on Artificial Intelligence (AI), the IUCT-Oncopole and the IRT Saint Exupéry have published two articles in prestigious international journals. The first, published in The Oncologist, concerns the results of phase I of the promising STERIMGLI clinical trial, which aims to evaluate a new strategy combining radiotherapy and immunotherapy. Thanks to AI algorithms, the identification of new markers (biological, molecular, imaging, etc.) could also soon enable doctors to select patients who will be receptive to this new combined treatment. (Read the article)

Initial work, focusing on the ability of AI to recognise or not molecular biological characteristics (methylation of DNA repair enzymes) of glioblastomas from MRI data, was the subject of the second article published in Cancers. (Read the article)

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.
The Oncogeriatics OCC participates, with the various organ committees and in partnership with DIALOG Gerico, in studies concerning the application of treatments in elderly subjects.

ASSESSING THE CONSEQUENCES OF AGE

Impact of Chemotherapeutic Treatments in Patients Aged 75 Years and Over Treated for Lymphoid Hematological Malignancy (LYMPHOLD)
Coordinator: Dr Laurent Balardy
The aim of the study is to assess the prevalence of functional decline in elderly patients treated with chemotherapy or immunochemotherapy for lymphoid hematologic malignancies. For this purpose, each patient benefits at inclusion (D0) of a standardized gerontological evaluation, and 3 and 6 months post-inclusion (NCT05101759).

Onco-ICOPE: ICOPE Program Feasibility in the Management of Myeloma Patients Over 70 Years.
Coordinator: Gilles Bourgade
This project proposes to adapt monthly the existing ICOPE (Integrated Care for Older People) MONITOR program for older patients with cancer for. This adaptation aims to detect earlier functional decline and prevent loss of autonomy (NCT06247189).

The WHO ICOPE Program to Monitor Intrinsic Capacity in Older Adults with Cancer
Coordinator: Dr Zara Steinmeyer
The ICOPE program, currently deployed in the Occitanie region, could be adapted to extend and improve care pathways for elderly cancer patients. Deployment of the ICOPE program would not only preserve patients' intrinsic capacity and autonomy, but also facilitate the organization of integrated care and city-hospital coordination during treatment. Read the article

NIVOREN RESULTS

Safety and efficacy of nivolumab in elderly patients with metastatic clear cell renal cell carcinoma: Analysis of the NIVOREN GETUG-AFU 26 study
First autor of NIVOREN elderly section : Dr Loïc Mourey
The NIVOREN trial, initiated by UNICANCER, is a Phase 2 interventional study designed to assess the safety and efficacy of Nivolumab in patients with metastatic clear cell renal cell carcinoma. This study, conducted on 720 patients including 205 over 70 years of age, demonstrated that Nivolumab treatment had a higher rate of grade 3 to 5 treatment-related events, but manageable toxicity in patients over 70 years of age with sustained activity (NCT03013335).

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. Read the article

PRESIDENCY OF DIALOG

Since 2022, 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. Dr Loïc Mourey is also co-president of the SoFOG Scientific council, alongside Dr Anne-Laure Couderc and Dr Bérengère Beauplet. 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).

- Link 1
- Link 2
- Link 3

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.

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). Read the publication

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).

High intensity program et non moderate
The study began in July 2022 and has so far enrolled 44 patients. At this stage, no significant differences between the groups were observed for any of the variables studied, making it impossible to conclude that there was an effect of exercise intensity. The results of the study show an significant improvement of insulin sensitivity, lipid profil and blood pressure during the 6 months programs. Evolutions show an improvement in the metabolic tolerance of certain anti-cancer treatments. Blood cortisol and physical condition are altered by treatment and hospitalization but less for the high intensity group. Ancillaries studies will investigate the metabolomic and microbiota signatures of the children to give further axis of analysis.

Ear, Nose and Throat OCC

Coordinators: Pr Sébastien Vergez & Dr Anouchka Modesto

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

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

ANTI-CANCER VACCINE: FIRST RESULTS ENCOURAGING

Coordinator: Pr Jean-Pierre Delord
Engaged in research against head and neck cancers, the Oncopole teams presented the first encouraging results of the phase I clinical trial of the TG4050 vaccine at the ASCO 2023 Congress. Based on the identification of the neo-antigens located on the cell surface, the individualized vaccine aims both to induce a lasting immune response, in addition to active treatments, and to prevent recurrences. All patients who received the vaccine had an immune response, and those with head and neck cancer had no relapse. Phase II has been launched to verify the effectiveness of this therapeutic strategy.

ASSESSING CLINICAL BENEFIT

Investigators: Dr Anouchka Modesto
In recent years, several immune checkpoint inhibitors have been approved to treat various solid tumors, including metastatic esophageal cancer. To assess the effectiveness and clinical benefit for these patients of adding an anti-PD-L1 antibody to chemoradiotherapy (CRT) and then continuing it as maintenance therapy, radiotherapist Dr. Anouchka Modesto is coordinating the phase II ARION study whose initial results have been published in BMC Cancer.
Read the article

BIOFACE : FIRST UNIVERSITY-HOSPITAL RESEARCH PROJECT (UHR) IN OCCITANIE

Coordinator: Pr Agnès Dupret-Bories
As part of France 2030 (a national research investment plan) the Toulouse BIOFACE project, led by Prof. Agnès
Dupret-Bories and the Toulouse University Hospital, won the call for proposals in University-Hospital Research in Health.
Surgery is the optimal treatment for the oral cavity and frequently requires the removal of a segment of the mandible or maxilla. To limit the aesthetic and functional after-effects, bone reconstruction is carried out during the same operation using a free bone flap. The operations are lengthy, with high morbidity rates, complications, aesthetic and motor sequelae, and significant risks of failure. These major operations are not accessible to all patients.
The BIOFACE project will develop an innovative solution based on preliminary data to solve a clinical problem for which current solutions are sub-optimal: immediate and personalised bone reconstruction in one step while limiting morbidity. To achieve this, 4 new custom-made medical devices (3D printing) will be developed and/or improved. This project aims to improve patients' quality of life by radically changing surgical procedures. One of BIOFACE's other objectives is to develop a new concept in pre-clinical trials by limiting the use of animal experiments (One Health/ One Medicine approaches).
This 5-year project ranges from in silico to multi-centre clinical trials.
Seven partners are involved in this project, including academic partners (Inserm UMR 1121 in Strasbourg, CIRIMAT in Toulouse), industrial partners (Cerhum, Spartha Medical, Materialise, Oncovet Clinical Research) and hospital partners (IUCT-Oncopole). This project, worth almost €13m, has received funding of €4.395m.

RECONCILING EFFICACY AND QUALITY OF LIFE

Coordinator:Dr Victor Sarradin
50% of patients treated for ENT cancer suffer a relapse, which is then treated with immunotherapy, often combined with chemotherapy, a source of toxicities. Inspired by the treatment of lung cancer, Dr Victor Sarradin, a medical oncologist at Oncopole, will be coordinating the 'REDUCE' project. The aim is to reduce the number of cycles of combined chemotherapy + immunotherapy, from six to four, before maintenance treatment with immunotherapy alone, in order to reduce side effects in these often fragile patients, while maintaining the effectiveness of the treatment. If the results are positive, this study will lead to a reduction in acute and late toxicities, with the ultimate aim of improving patients' quality of life.

Sarcoma OCC

Coordinator: Dr Anne Ducassou and Dr Thibault Valentin

Main collaborations:
Several members of Sarcoma OCC also belong to ONCOSARC team at the CRCT (Coordinator: Dr Frédéric Chibon)

EXPERTISE

Sarcoma OCC is one of the driving force of Toulouse Adolescent / Young Adults (AYA) team, and aims to develop the access to phase1 one studies for these patients.

SPECIFIC THEMES IN RADIOTHERAPY

Adaptive radiotherapy: Results
Coordinator: Dr Anne Ducassou
Results of a project about preoperative adaptive radiotherapy, first presented as a medical thesis, were published in 2023 in Radiology and Oncology journal. They propose a new method, very simple to use in practice, to detect patients who will need a replanification. Read the article

Launch of MEDISARC-RS in early 2024
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 patient was included in December 2023 and study is on-going.

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 is on-going
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 soft-tissue sarcomas defined as high-risk by CINSARC, a molecular signature identified in 2010 by Dr Frédéric Chibon (NCT04307277).
MIRAS (PRT-K 2018)
This multicenter translational cohort aims to characterize the clinical and biological features of rare soft tissue sarcoma (NCT04459234).
SAMHY 2 project and PAN-DPC project : aiming to search «hybrid» (cancer / immune) circulating cells in patients with sarcoma and other cancer subtypes.

Breast cancer OCC

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

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

TRIPLE-NEGATIVE BREAST CANCER

Spatial organization of lymphocytes
Project carried out in coordination with DynACT team at the CRCT
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.

ADC Low
Coordinators: Pr Florence Dalenc & Dr François Poumeau
Presented at the San Antonio Breast Cancer Symposium (USA) last December, ADC Low is the name of the largest national retrospective multicenter study evaluating the efficacy of one conjugate antibody following another in patients with metastatic breast cancer. Led by a young oncologist, Dr. François Poumeaud, under the direction of Prof. Florence Dalenc, the study included 179 patients.
The results were presented and praised at the San Antonio Breast Cancer Symposium last December.
Find out more about ADC Low

Read the article

METASTATIC BREAST CANCER

Coordinators: Pr Florence Dalenc, Dr Laura Keller & Dr Frédéric Chibon
Based on 100% Toulouse-based research by the CRCT's Oncosarc team, the new DP-Metabreast study aims to identify new therapeutic targets.
Using liquid biopsies, the team aims to prove the tumoral origin of so-called double-positive cells (expressing epithelial and immune markers) to understand their role in tumor dissemination and better characterize them.
This study will be offered to 60 Oncopole patients treated for metastatic breast cancer.

OBESITY & BREAST CANCER

Impact of Obesity on the Composition of the Tumour Microenvironment in Luminous Breast Cancers
Coordinator: Pr Muller-Staumont Catherine
The aim of this project is to study the link between obesity and the prognosis of luminal breast cancer (LBC). Clinical data shows that obesity increases both overall and specific mortality, as well as the risk of recurrence of LBC. Breast cancer develops in breast adipose tissue (BAT). The hypothesis is that the distinct and aggressive nature of LSC in obese patients is due to changes in the tumour microenvironment caused by alteration of the surrounding TAM.
To achieve its objectives, this project relies on the interdisciplinary synergy of 4 teams of researchers, clinicians and pathologists with internationally recognised expertise in breast cancer, in the adipose tissue/cancer dialogue, in the heterogeneity of the tumour microenvironment in breast cancer, with a specific interest in cancer-associated fibroblasts (CAF), and in the pathophysiology of obesity and its complications. This project uses innovative technologies in single cells, multimodal imaging and co-culture models. It benefits from access to retrospective cohorts of annotated tumours with long clinical follow-up.
The objectives are to determine how obesity modifies: i) the cellular composition of the ASC microenvironment; ii) the metabolites and soluble factors secreted by the TAM and the metabolic dialogue between adipose tissue and cancer; iii) the aggressiveness of tumours using innovative in vitro coculture models. The prognostic impact of the new targets identified will be validated on retrospective clinical cohorts. A representative of patients' associations will sit on the steering committee.
This interdisciplinary approach to adipose tissue will enable new therapeutic strategies targeting the tumour microenvironment to be identified for the treatment of luminal breast cancers in populations stratified by obesity.

Supportive Oncology Care OCC

Coordinators: Dr Nathalie Caunes-Hilary

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 (Find out more). Dr. Antoine Boden has published a review of the literature on the subject. See the article

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 - see article); on the flexibility of end-of-life legislation (Roxane Delpech and Pr Bettina Couderc - see article); and on the temporal challenges of deep and continuous sedation (Pr Bettina Couderc and Dr Nathalie Caunes-Hilary - see article).

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.

Department of Internal Medicine

Coordinator: Dr Thibault Comont & Pr Odile Rauzy

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

MISSIONS

The Department of Internal Medicine's expertise covers myelodysplastic syndromes, infections in immunocompromised patients, and rare immunohematological diseases (autoimmune cytopenias, inherited red cell disorders, primary immunodeficiencies, histiocytosis). It is a referral center for immunological manifestations associated with hemopathies and complications related to immunotherapy. The department 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 myelodysplastic syndromes. The results of the preliminary studies are scheduled for 2024. PMID 38575672 - PMID 34151423

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). PMID 38071510 - PMID 34651299 - PMID 33164099

RARE IMMUNO-HEMATOLOGICAL DISEASES

The Department of Internal Medicine is one of four national reference centers for immune cytopenias (CeReCAI) since 2016. The department is also a Center of Competence for hereditary immunedeficiencies and for histiocytosis. See the article

HEMOGLOBIN DISEASES

Coordinator: Dr Pierre Cougoul
The Internal Medicine department was labelled referal center for inherited red blood cell disorder in 2023.
Among the different center's projects, IUCT Oncopole is a national observatory center for oncohematological diseases in people with sickle cell anemia (SICKLONE project). In collaboration with INSERM, we conduct the "Il Padre" study which investigates thrombo-inflammation mechanisms involved during vaso-occlusive crisis. The center participates in academic (OSONE, TOCIACS) and industrial trials. In 2023 two first patients were involved in PHRC DREPARIC (APHP Trial studying reduced conditioning regimen in bone marrow allograft for sickle cell patients).

IMMUNE RELATED TOXICITIES

Coordinator: Dr Valerian Rivet
The department is responsible for the monthly multidisciplinary meeting for the management of patients presenting with immunotherapy toxicities and manage patients in collaboration with oncologists and organ specialists. In collaboration with Montpellier University, Dr V Rivet participate in teaching on immunology through an inter-university diploma.
PMID 38515568 - PMID 37138674

Technical medical units

Department of Surgery

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

CERVICAL CANCER

Coordinator: Pr Alejandra Martinez
Under the aegis of ARCAGY-GINECO and the European Network of Gynecological Oncological Trial Groups (ENGOT), this project is the second largest international study of gynaecological cancer surgery after SENTICOL. PAROLA (PARa-aOrtic LymphAdenectomy in Locally Advanced Cervical Cancer), which has been awarded PHRC-K funding in 2021-2022, is a phase III study investigating the role of lumbo-aortic curage in advanced cervical cancer, in order to adapt radiotherapy fields more precisely according to lymph node staging.The PAROLA study opened for enrolment in 2023.

Coordinator: Dr Gwenaël Ferron
The international SHAPE study, led in France by Dr. Gwénaël Ferron, has shown that less invasive surgery (simple hysterectomy) is as effective (reduced complications, better quality of life) as complete hysterectomy for women with early cervical cancer. Presented at ASCO 2023, the results of the SHAPE study have also been published in the international journal The New England Journal of Medicine.

ORAL CAVITY CANCER

The aim of the retrospective single-centre MIDLINE study was to determine the indication for prophylactic contralateral cervical curettage in patients with squamous cell carcinoma of the oral cavity or oropharynx approaching the midline without crossing it. Oropharyngeal tumour origin (particularly basilingual) and homolateral cN+ lymph node status were the main risk factors for contralateral occult lymph node involvement, but not midline involvement by the primary tumour (read the article).

BREAST CANCER

Autologous fat transfer (AFT) is widely used to improve the outcome of reconstructive breast surgery, but its safety is controversial. The aim was to evaluate the oncological safety of AFT in a homogeneous population of patients who had undergone total mastectomy with immediate reconstruction for breast cancer.
Read the article : Oncologic safety of autologous fat grafting in primary breast reconstruction after mastectomy for cancer (Anne-Sophie Navarro, Donia Omalek, Léonor Chaltiel, Charlotte Vaysse, Thomas Meresse, Dimitri Gangloff, Eva Jouve, Gabrielle Selmes)

Department of Medical Physics

Director: Dr Laure Vieillevigne
Co-director: Grégory Hangard

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

START OF A NEW RADIOTHERAPY FACILITY

First treatments on the Halcyon 6 started on the 9th January 2023. This machine enables intensity modulated treatments with fully integrated imaging and surface guided radiation therapy.
The project leader was Grégory Hangard and the physicists Aurélie Tournier, François Xavier Arnaud, and Marine Stadler were in charge of the machine's commissioning.

MAJOR MILESTONES ON TWO GOING INNOVATIVE PROJECTS WITH AIRBUS

Coordinator : L. Vieillevigne
Two projects launched in the frame of the MoU with Airbus are in progress on:

Prediction of breakdowns in TomoTherapy machines (Accuray)
Development of an innovative approach capable of proactively detecting early signs of machine failure, by combining advanced machine learning methods with in-depth expertise in the field of radiotherapy
Master's intership management

Optimization of appointment scheduling for RTE patients
Successful application for the « AI for Health » call for projects funded by the Occitanie Region and ANITI

DEFENSE OF TWO THESIS IN MEDICAL PHYSICS

Alexia Delbaere - Defense on 28/02/2023
Thesis Title: Metrological Formalism for Determining the Absorbed Dose in Heterogeneous Media for High-Energy Photon Beams
Thesis Advisor: Laure Vieillevigne

Quentin Maronnier - Defense on 20/12/2023
Thesis Title: Development of Innovative Tests and Procedures for the Design and Evaluation of a New PET/CT Technology: From Phantom to Human
Thesis Advisor: Olivier Caselles

INTERNATIONAL TRAINING

The Dosimetry Schools are held worldwide, but this was only the second time that this training for medical physicists took place in France, and it was held at the Oncopole. The first session organized in France was in 2018, also at the Oncopole.
Several sessions were led by members of the Medical Physics team. Participants had the opportunity to explore the latest technological advances from theory to practice. Practical workshops were conducted on Saturday using the various accelerators at the Oncopole.

Radiotherapy Department

Coordinator: Pr Elizabeth Moyal

Main collaborations:
Interconnections with the RADOPT team 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.

ASSESSING CLINICAL BENEFIT

Coordinator: Dr Anouchka Modesto
In recent years, several immune checkpoint inhibitors have been approved to treat various solid tumors, including metastatic esophageal cancer. To assess the effectiveness and clinical benefit for these patients of adding an anti-PD-L1 antibody to chemoradiotherapy (CRT) and then continuing it as maintenance therapy, radiotherapist Dr. Anouchka Modesto is coordinating the phase II ARION study whose initial results have been published in BMC Cancer.
(Read article)

CONSOLIDATIVE RADIOTHERAPY

Coordinator: Dr Jonathan Khalifa
For patients with a metastatic urothelial carcinoma not progressing after 1st-line chemotherapy, Dr. Jonathan Khalifa is coordinating the randomized phase II BLAD-RAD 01 trial to evaluate the benefit of adjuvant radiotherapy on the bladder and residual oligometastases in addition to standard avelumab maintenance therapy. Conducted on a national level, the study to date includes 28 patients out of the 130 expected.

IA PARTNERSHIP WITH IRT ST-EXUPÉRY

Coordinator: Pr Elizabeth Moyal
Since 2022, IUCT-Oncopole and the Institut de Recherche Technologique (IRT) Saint-Exupéry, an expert in AI for mission-critical systems, have been collaborating around an AI-focused partnership agreement. Several projects have already been launched:

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

- Using AI to predict MGMT promoter methylation (prognostic factor)

PARTNERSHIPS

Synergy between aeronautics and medicine
Improving the planning of radiotherapy sessions — crucial for speeding up patient care — is a major focus for many researchers. This optimization aims to allocate patients to different machines according to criteria of urgency, pathology and patient well-being, along with technical and dosimetric constraints. An initial feasibility study, conducted with Airbus and incorporating AI, transposes approved aerospace solutions to cancer care. Results are due to be published shortly.

Prediction
When using complex radiotherapy equipment, component breakdowns can occur, complicating patient care. To prevent these interruptions of varying duration, the Oncopole has signed an unprecedented partnership with Accuray and Airbus to co-develop a failure prediction system based on machine learning and AI.

Oncohematology Laboratory

Coordinator: Pr Véronique De Mas

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

REFERENCE LABORATORY

The laboratory is a reference unit for the GRAALL (Adult Acute Lymphocytic Leukemia), CAALL-F01 (Childhood Acute Lymphocytic Leukemia), the FILO (French Innovative Leukemia Organisation) and IFM (Intergroupe Francophone du Myélome) protocols.

HYBRID INTELLIGENCE IN FLOW CYTOMETRY

Two studies by Drs Inès Vergnolle and Alban Canali coordinated by Dr François Vergez, used artificial intelligence software to improve lymphoma diagnosis and follow-up of AML patients. Dr I. Vergnolle has shown through Random Forest analyses that the CD43 marker may be more predictive of lymphoma type than the Matutes score (read the article). Dr. A. Canali used clustering methods to show that the search for rare post-induction leukemic stem cells was highly predictive of AML relapse (read the article). The combination of cytometrists' expertise and computer power in a hybrid intelligence system has made it possible to identify critical cytometric markers in various hematological disorders.

FAMILIAL AND GENETIC HEMOPATHIES

Dr Laetitia Largeaud, Pr Eric Delabesse and Pr Marlène Pasquet showed that germline GATA2 mutations which predispose to myeloid malignancies progressively acquire specific somatic mutations that are associated with clinical/hematological evolution of GATA2 syndrome. This study may help clinicians in their management of patients.
Read the article

RESISTANCE TO RUXOLITINIB

JAK2 inhibitor Ruxolitinib show important benefits in patients with myeloproliferative neoplasms, however the efficacy is limited. Dr Carine Joffre (METAML team, CRCT) and Pr Véronique De Mas have identified phosphatase PP2A-dependant autophagy as one of possible mechanism for resistance to treatment.
Read the article

GENOMIC STUDIES IN MYELOMA

Work coordinated by Prof. Hervé Avet-Loiseau & Prof. Jill Corre on the cytogenetic abnormalities involved in multiple myeloma resulted in three major publications in 2023. The first confirmed the deleterious impact of the deletion 1p32 on prognosis and identify an ultra-high risk entity for patients displaying a biallelic deletion (read the article).
The second study showed that t(14;16) is very frequently associated with other high-risk cytogenetic abnormalities such as del17p, gain(1q) or del(1p32). Isolated t(14;16) was very rare and seemed not to have any prognostic impact (as the number of cases is very small, this remains to be confirmed). Nevertheless, its association with other anomalies, particularly 1q gain, should be considered high-risk. (read the article).
These two studies had a strong impact on the new definition of high genetic risk myeloma from the International Myeloma Society.
The third study demonstrated that many patient at diagnosis have little aggressive subclones undetectable by DNA sequencing on bulk, but detectable by single cell analysis. Some of them have already a poor impact on outcome, and become dominant at relapse (read the article).

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 AI-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.

Resuscitation and Continuing Care Unit

Coordinator: Dr Muriel Picard and Dr Guillaume Ducos

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

PROSPECTIVE MULTICENTER STUDIES

PIC 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, 2015-022) and PIC (coordinator Dr Virginie Lemiale, sponsor AP-HP, P150961) – which respectively are examining the impact on mortality at D90 of de-escalation of antibiotic therapy in hematologic cancer patients admitted to the ICU for septic shock or severe sepsis, and the impact on mortality of adding corticosteroid therapy to the treatment of severe pneumocystis in immunocompromised patients. Further plans to participate in multicenter studies within the Grrr-OH are underway.

OSONE STUDY

Coordinator: Dr Sihem Bouharaoua
Prospective multicentre, randomised, open-label, multi-stage study with three stages (pilot, activity and efficacy) and four arms (one control arm and three intervention arms) involving 35 French centres (P180303J). The primary objective is to evaluate the safety and efficacy of high-flow oxygen therapy in patients presenting a vaso-occlusive crisis at risk of secondary acute chest syndrome. The study is being coordinated by Prof Mekontso Dessap (Hôpital Henri Mondor) and conducted in collaboration with the IUCT-O Internal Medicine Department (Dr Cougoul).

STUDY OF ONCOGERIATRIC PROGNOSIS IN INTENSIVE CARE UNITS

Sponsor: CHU Toulouse
Coordinator: Dr Guillaume Ducos
Single-centre retrospective study of the prognosis of elderly patients (≥ 75 years) with haematological malignancies admitted to intensive care from 2014 to 2023. Data collection in progress (Marine Ferrasse).

HEMO² STUDY

Sponsor: CHU Toulouse
Coordinator: Dr Muriel Picard
National multicentre retrospective study (Grrr-OH) on the prognosis of patients with haematological malignancies admitted to intensive care for haemorrhagic shock from 2014 to 2023 (RnIPH 2023-062). Data collection in progress (Léo Tawil).

MIVRE STUDY

Sponsor: CHU Toulouse
Coordinator: Anne Ferré, Bettina Brefeil & Manon Foucreau
The MiViRe study is a para-medical study by the IUCT-O intensive care unit, funded by the SFAR, the aim of which is to evaluate the impact of an informative video on the experience of an intensive care stay in patients requiring an intensive care stay after major carcinological surgery. The ICU team wanted to demonstrate that access to an informative video covering the details of an ICU stay could reduce anxiety levels and improve overall satisfaction and perception of the ICU stay.

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