CONGRESS BOOKLET

1st Young Scientist Cancer Congress (YS2C)

New research strategies for cancer therapy – from bench to bedside

Toulouse, France - October 05, 2023

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Welcome!

The Centre de Recherche en Cancérologie de Toulouse (CRCT) postdocs association was created in 2022 by Benoît Aliaga, Chloé Bessière and Steffen Fuchs. It gathers the more than 30 postdocs who are currently present in our research center. We decided to organize the 1st Young Scientist Cancer Congress (YS2C) of the Cancéropôle Grand Sud Ouest (GSO) on October 5, 2023 at the Oncopole, Toulouse. This congress has been organized with the help of many volunteers, and we would like to thank them.

The main goals of this day are to promote the work of the GSO postdocs and young clinician scientists, to network, and to optimize their career paths. To achieve our goals, we decided to open the conference to the whole scientific community, which are researchers and clinicians of all career levels.

This day will alternate presentations by internationally renowned keynote speakers, presentations by postdocs from the GSO, application-focused presentations by two companies IntegraGen and Mission Bio, and a presentation from an editor of *Nature Communications* about scientific publishing and peer-reviewing.

We hope that you will enjoy this day!

The organization committee:

- Dr. Benoît ALIAGA, PhD; CRCT, Toulouse benoit.aliaga@inserm.fr
- Dr. Chloé BESSIERE, PhD; CRCT, Toulouse chloe.bessiere@inserm.fr
- Dr. Benjamin BONNARD, PhD; BRIC, Bordeaux benjamin.bonnard@inserm.fr
- Dr. Steffen FUCHS, MD; CRCT, Toulouse, Charité-University Hospital Berlin, Germany steffen.fuchs@inserm.fr
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-Dr. Julie RIPOLL, PhD; LIRMM, Montpellier julie.ripoll@lirmm.fr
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1st Young Scientist Cancer Congress

Welcome from the CRCT director and member of the GSO's steering Committee

According to current norms, postdoctoral researchers, often referred to as postdocs, are typically viewed as young scholars only pursuing research, having their heads down trying to beat a deadline and diligently preparing for careers in academia or industry.

Well… the postdoc community of the CRCT definitely challenges this conventional perception. Our Postdocs play an integral role making the CRCT the flourishing institution that it is, ranging from mentoring undergraduates to engaging in cutting-edge laboratory research and producing top-notch research papers. What truly sets them apart is their exceptional dedication to fostering a sense of unity within our institution. As the Director of the CRCT, I find myself profoundly impressed by their enthusiasm, dynamism, and their remarkable effectiveness in organizing the first-of-its-kind young scientists cancer congress you will attend today, now welcoming more than two hundred attendees including prominent key opinion leaders. This event will serve as a unique platform for connecting young and talented research scientists, not only from within our borders but also from abroad. Moreover, it will facilitate interactions with promising junior research clinicians, thanks to the generous support of IUCT-Oncopole. I take immense pride in the fact that this event is set to become a staple in our calendar, extending its reach to encompass the entire postdoctoral community of the Canceropole Grand Sud Ouest (GSO). As an active member of the GSO's steering committee, I extend my gratitude to them for inclusively incorporating colleagues from Bordeaux and Montpellier, thereby strengthening regional scientific collaboration and development. I extend my best wishes to all those attending for a rewarding day of scientific exchange and networking.

Sincerely yours

Dr. Pierre Cordelier, Director of the CRCT and member of the GSO's steering Committee

Welcome from the IUCT-O director

Dear colleagues,

We are delighted to welcome you to Oncopole for this Young Researchers' Day.

I would like to take this opportunity to thank our young colleagues for their commitment in the organization of this meeting. The idea for this day is theirs. All we had to do was encourage them to continue. Their enthusiasm did the rest!

It was in this spirit that our Oncopole project in Toulouse was built. It's the desire to succeed by sharing the demands of high-level scientific research and strong interaction with those who care for patients… and demonstrate that the ideas were the right ones. Only the right ideas can cure cancer. And if "our" young people support this vision, then we'll get there! So I wish "long life" to this wonderful initiative.

Welcome to Oncopole!

Prof. Jean-Pierre Delord, Director of the IUCT-O

INSTITUT UNIVERSITAIRE DU CANCER DE TOULOUSE
Oncopole

Welcome from the CARe program director

As Deputy Director of the « Cancer, Ageing and Rejuvenation» (CARe) Graduate School, I would like to reiterate my support for this wonderful initiative, the « First Young Scientist Cancer Congress » (YS2C). It is firmly in line with the Graduate School program, because of its innovative, transdisciplinary, and international nature. Like CARe, this Congress aims to promote top-quality teaching and research in the field of cancer. The lectures you will be attending on this day will give you an overview of the current State of the Art, with workshops of scientists from all backgrounds, from bench to bedside and back. Working on innovative and complementary themes in both the private and public sectors, in France and abroad, this new generation of researchers aims to develop practices and exchanges in the field of future cancer research.

These transdisciplinary and international aspects are the “raison d'être” of CARe, which is why it seemed natural to me to invite all our students to attend this extremely rich day. It is vital that they realize the importance of international collaboration in their future careers, because this is the path they have chosen to take by joining our Graduate School program.

I sincerely hope that this edition of the YS2C is the first of many more that some of you may take part in the years to come.

I thank very much the organizers and speakers for this fantastic workshop.

Prof. Bruno Segui, Deputy Director of the CARe program

CARe
Cancer, Ageing & Rejuvenation
Graduate school

The YS2C organizing committee warmly thanks the academic and industrial sponsors who agreed to take part in this first edition!

PRACTICAL INFORMATIONS

Prizes for best oral and poster presentations

Several competitions are organized to reward young researchers/clinicians (PhD students, post-docs, interns):

- Best oral presentation awarded by Integragen and Merck
- Best 2 posters by NeoVirtech
- Best oral and poster presentations in pediatric oncology awarded by the association Enfants Cancers Santé
- Best poster presentation in cancer bioinformatics awarded by the Société Française de Bioinformatique (SFBI)

Social media

When posting on social media (Twitter/X, LinkedIn) about the conference, please use our hashtag **#YS2C_GSO.**
Follow our Twitter/X accounts: @Crct_Postdoc, @crctoncopole, @IUCTOncopole, @CareGraduate and @CanceropoleGSO

WiFi

You can connect for free to the open network “Hotspot-IUC”
(no password or account is needed).

Location of coffee breaks, lunch and Icebreaker

The coffee break will be provided close to the IUCT-O amphitheater.
Lunch will be provided in the atrium (follow the indications).

Directly after the closing ceremony, we will have the Icebreaker at the CRCT (follow the indications).

Badges

Please return your badge at the end of the congress to the provided boxes.

Questions?

Don’t hesitate to contact the congress organizers via liste.crct-postdocday@inserm.fr.

PROGRAM

8:30 - 9:00	Registration + Welcome coffee
9:00 - 9:12	Welcome address
Session 1: Cancer epigenomics and beyond	
09:15-10:00	**Manel Esteller**, Josep Carreras Leukaemia Research Institute (IJC), Barcelona, Spain *Cancer Epigenomics and Epitranscriptomics with a Single-Cell Twist.*
10:00-10:20	**Oriana Villafraz**, Institut de Recherche en Cancérologie de Montpellier, France *Metabolic networks regulated by Mut-p53: an integrated approach to design new therapeutic strategies*
10:20-11:10	Coffee break
11:10-11:20	Tech Talk by **Elodie Lallet**, IntegraGen, Evry, Paris *From tumor to treatment, OncoDEEP® kit : a comprehensive oncology NGS panel including powerful bioinformatics tools*
Session 2: Single-cell technologies and their applications to dissect cancer heterogeneity	
11:20-11:40	**Pierre-Paul Axisa**, Cancer Research Center of Toulouse, France *Dissecting natural killer cells dysfunction in multiple myeloma*
11:40-11:50	Tech Talk by **Gema Fuerte** Field Application Scientist Manager, Mission Bio, CA, USA *Unleashing the Power of Single-Cell Multi-Omic DNA and Immunophenotype Profiling: Revolutionizing Precision Medicine and Shaping Next-Generation Therapies*
11:50-12:00	**Hervé Avet-Loiseau**, CRCT, IUCT-O, Toulouse, France *Early clonal study in Multiple Myeloma*
12:00-14:15	**Poster session, company desks (present during the whole day), lunch buffet and Physician's corner**

Session 3: Cancer plasticity and heterogeneity	
14:15-15:00	**Olivier Delattre**, Institute Curie, Paris, France *Ewing sarcoma, a paradigm for cell reprogramming in cancer*
15:00-15:20	**Adrien Latge**, Institut Universitaire de Cancer Toulouse-Oncopole, France *68Ga DOTATOC PET-CT and 123I-mIBG scan discordances in a refractory case of pediatric neuroblastoma: tumor heterogeneity with implications for patient management*
15:20-15:40	**Alix Bouillin**, Institut du cancer de Montpellier *New biomarkers in liposarcomas: a metabolic approach*
15:40-16:10	The editor's perspective: **Kathryn McGinnis**, Associate Editor, *Nature Communications*
16:10-16:40	Coffee break
Session 4: Cancer dependencies and drug development	
16:40-17:00	**Julie Giraud**, ImmunoConcEpT Bordeaux, France *Expansion of TREM1+ regulatory myeloid cells in steatohepatitis-HCC associates with poor prognosis and resistance to immune checkpoint blockade*
17:00-17:20	**Clara Maria Scarlata**, Cancer Research Center of Toulouse, France *T-cell exhaustion is an independent predictive biomarker of clinical outcome in high grade serous ovarian cancer regardless of homologous recombination deficiency status*
17:20-18:05	**Francesco Iorio**, Wellcome Sanger Institute, Cambridge, UK; Human Technopole, Milano, Italy *Optimisation and drug-discovery oriented analyses of CRISPR-Cas9 screens.*
18:05-18:20	Closing remarks and Ceremony of poster/oral communication awards
Get-together/Icebreaker with the keynote speakers and the postdocs (at CRCT)	

THE PHYSICIAN CORNER

One of our aims is to bring young clinicians and researchers together. This will foster exchange and potentially start future collaborations, all for the sake of translational research and ultimately for the patient's benefit. This is why we will have a dedicated space during the lunch break and poster session, "the physician's corner", where informal discussions between clinicians and researchers can happen in a relaxed atmosphere. Our panel of clinicians will be interdisciplinary having different specialities, such as pathology, breast cancer, radio-oncology, biostatistics and early clinical trials. This will provide you with plenty of possibilities to discuss. Use this opportunity and just come around!

KEYNOTES SPEAKERS

The YS2C organizing committee warmly thanks the keynote speakers who agreed to take part in this first edition.

Dr. Manel Esteller, MD, Ph.D

Director, Josep Carreras Leukemia Research Institute

Manel Esteller graduated in Medicine from the Universidad de Barcelona in 1992, where he also obtained his Ph.D. degree specializing in molecular genetics of endometrial carcinoma, in 1996. He is the Director of the Josep Carreras Leukaemia Research Institute (IJC), Chairman of Genetics in the School of Medicine of the University of Barcelona, and an ICREA Research Professor. His current research is devoted to the establishment of the epigenome and epitranscriptome maps of normal and transformed cells, and the development of new epigenetic drugs for cancer therapy. Author of more than 600 original publications in peer-reviewed scientific journals, 24 of them categorized as "Highly Cited Paper". Dr. Esteller has the highest total impact factor and the highest number of citations (81,783) among biomedical scientists in Spain. Dr. Esteller is considered among the Top 0.01% of World Scientists based on Impact by both the Stanford University (METRICS) and the Web of Science Group-Clarivate Analytics. He is also a Member of numerous international scientific societies, Editorial Boards, and a reviewer for many journals and funding agencies. In 2022, his discovery of cancer type-specific DNA hypermethylation profiles was selected as a Landmark Article in Cancer Research by the AACR and the National Cancer Act.

Dr. Olivier Delattre MD, Ph.D

Director at Cancer, Hétérogénéité, Instabilité et Plasticité – U830 – Institut Curie

Olivier Delattre, MD, PhD was trained in pediatric oncology and in genetics. His research area mainly investigates the genetics and biology of pediatric cancers. In particular, his laboratory has identified the genetic alterations of a variety of childhood cancers, including the EWS-FLI1 rearrangement in Ewing sarcoma, the SMARCB1 inactivation in rhabdoid tumors, the ALK activation mutation in neuroblastoma and the BCOR-CCNB1 fusion in Ewing-like sarcoma. He has also contributed to identifying major tumor predisposing mutations or genetic susceptibility factors in neurofibromatosis type II, rhabdoid syndrome predisposition, neuroblastoma, and Ewing sarcoma. His lab also has a strong interest in deciphering the cellular origin of pediatric cancers and particularly Ewing sarcoma, neuroblastoma, and rhabdoid tumors. Globally, the interest of his lab is to further understand the interplay between genetic abnormalities and the specific background of the cell of origin. Olivier Delattre is a member of EMBO since 2011 and of Academia Europea since 2012. He received numerous awards, including the Eurocancer Award in 2007, Charles Oberlin Award in 2009, the Leopold Griffuel award in 2016, the Grand Prix Inserm 2022, and was recently honored by the AACR-St. Baldrick's Foundation award for outstanding achievement in pediatric cancer research. Olivier Delattre is Director of the Cancer Biology and Genetics department at Inserm U830 and Director of the SIREDO center, a pediatric center of international stature that was created in 2017 at Institut Curie. SIREDO (French for Care, Innovation and research for children, adolescents and young adults with cancer) gathers researchers and physicians in the oncopaediatrics, adolescent, and young adult fields to bring new medications to patients as quickly as possible.

Dr. Francesco Iorio, Ph.D

Research Group Leader at Iorio Group, Computational Biology Research Centre, Human Technopole, Milan

Francesco Iorio is a Research Group leader in the Computational Biology Research Centre of Human Technopole (the life science institute in Milan, Italy). His group works at the interface of biology, machine learning, statistics, and information theory to understand and predict how genomic alterations and molecular traits from other omics contribute to pathological processes biological circuits' rewiring, and impact therapeutic responses in human cancers and other diseases. Their research aims to advance human health by designing algorithms, computational

tools, and novel analytical methods for integrating and analyzing pharmacogenomics and functional-genomics datasets to identify new therapeutic targets, biomarkers, and drug repositioning opportunities. The Iorio Group is contributing to creating a comprehensive map of all the genetic dependencies in human cancers and developing a computational infrastructure for translating this map into guidelines for early-stage drug development and precision medicine. They design, implement and maintain bioinformatics methods and original tools for the assessment of cancer preclinical models, the pre-processing, analysis, and visualization of genome-editing screening data for the in-silico correction of new-technology-specific biases in such data, and the optimization of single guide RNA libraries for pooled CRISPR-Cas9 screens and other experimental settings. They are also interested in big-data analytics, developing biomedical predictive models based on non-biomedical data, and computationally efficient constrained randomization strategies for testing combinatorial properties in large-scale genomic datasets and networks.

Dr. Kathryn McGinnis, Ph.D

Associate Editor, Nature Communications

Kathryn joined Nature Communications as an Associate Editor in 2021. She studied the role of steroids in brain cancer using bulk and single-cell RNA-sequencing during her PhD and subsequent post-doc at the University of Leeds, UK. She previously received her BSc in Immunology at the University of Glasgow and MSc working in industry within stem cell banking. Kathryn handles manuscripts surrounding the use of -omics technologies in cancer, particularly in the field of biomarkers of treatment response.

Gema Fuerte, M.Sc

Field Application Scientist Manager, Mission Bio

Mission Bio is a genomic company based in San Francisco which develops and commercializes a complete cutting-edge single-cell multi-omics offer which integrating genotype and phenotype, enabling researchers and clinicians to unlock single-cell biology to enable the discovery, development, and delivery of precision medicine. Tapestri platform allows Single-Cell multi-omics analysis with simultaneous detection of SNVs, CNVs, and cell-surface proteins, therefore enabling researchers to accurately characterize the mutational landscape of a

population and reveal the impact of co-mutations, DNA methylation and zygosity state on cell-surface protein expression.

Prof Hervé Avet-Loiseau, MD, Ph.D

CRCT, IUCT-O, Toulouse

Hervé Avet-Loiseau, MD, PhD, has been Head of the Laboratory for Genomics in Myeloma at the University Hospital Center of Toulouse, France, since September 2012. Before that he was the Head of the Haematology Laboratory of the University Hospital of Nantes, France, a position he had held since 2008. He received his medical degree with a specialization in paediatric haematology in 1990. After pursuing a postdoctoral fellowship in the laboratory of Dr. Joe Gray in San Francisco, CA, USA, he moved into the area of biological haematology in 1995 and subsequently specialized in cytogenetics. He received his PhD in 1998 and became Professor of Haematology in 2001. Professor Hervé Avet-Loiseau is highly involved in the Intergroupe Francophone du Myélome (IFM), and as the current Chairman he leads all biological studies. Most of his research studies are based on the analysis of genetic/genomic abnormalities observed in malignant plasma cells using different technologies, including fluorescence in situ hybridization (FISH), gene expression profiling, single nucleotide polymorphism (SNP) arrays, and next-generation sequencing (NGS).

Elodie Lallet, M.Sc

Key Account Manager, IntegraGen

Elodie Lallet joined IntegraGen in 2014 as a technology development engineer, where she worked on implementing new technologies and innovative solutions. In 2020, she joined IntegraGen's sales department, taking care of the South of France. IntegraGen, part of the OncoDNA group, is a French genomics and theranostics company specialized in precision medicine for cancer treatment. IntegraGen helps clinicians, researchers, and biopharmaceutical companies analyze molecular complexity, with the mission of providing access to precision medicine for the patient.

ABSTRACTS OF ORAL PRESENTATIONS

Dissecting natural killer cells dysfunction in multiple myeloma

Eve BLANQUART, Rüçhan EKREN, Bineta RIGAUD, Hélène DAUNES, Nadege CARRIÉ, Céline MAZZOTTI, Marine CUISINIER, Liliana LUCCA, Hervé AVET-LOISEAU, **Pierre-Paul AXISA**, Ludovic MARTINET

Centre de Recherche en Cancérologie de Toulouse

Multiple myeloma (MM) is an incurable cancer characterized by the proliferation of clonal, long-lived malignant plasma cells (PCs) within the bone marrow (BM). Genetic alterations are often present in PC clones from premalignant stages, which suggests that tumor-extrinsic factors govern the progression of pre-neoplastic lesions and response to treatment. T and natural killer (NK) cells become quantitatively and functionally altered in later stages of disease, thereby suggesting a relation between an impaired immune system and MM progression. NK cells represent a key compartment of the bone marrow and of the cytotoxic immune response against cancer cells, but so far the cellular changes associated with myeloma development remain poorly understood.

We counter-intuitively observed that increased NK cells frequency was associated with a poor clinical outcome in MM patients. Using single cell RNAseq phenotyping of bone marrow and blood from MM patients' samples vs healthy donors, we dissect cellular heterogeneity in the NK cells lineage. We observed an accumulation of NK cells with an inflammatory signature and a decreased expression of cytotoxicity-associated markers in MM patients, suggesting a dysfunctional state. This population is characterized by the loss of CD226 and CD16 surface molecules, which can be used as a proxy to isolate and characterize dysfunctional NK cells in vitro.

We confirmed the presence of dysfunctional NK cells in MM patients through in vitro experiments, where we observed a decreased expression of CD226 and CD16 compared to healthy controls. We also explore transcriptomic alterations of cytoskeleton-associated cellular processes, and their link with NK cells' motility and ability to find target cells in vitro. In conclusion, we unravel a dysfunctional NK state associated with clinical outcomes, which highlights the necessity to design therapeutic strategies to reinvigorate NK cells in MM context.

New biomarkers in liposarcomas: a metabolic approach.

Alix BOUILLIN[1,2], Sébastien CARRERE[1], Laurie GAYTE[2], Laetitia LINARES[2]
[1] Institut du cancer de Montpellier
[2] Institut de Recherche en Cancérologie de Montpellier

Liposarcomas (LPS) are rare soft tissue tumors of mesenchymal origin. The two main histological subtypes are well-differentiated (WD) and dedifferentiated (DD). Aggressive surgery is the only curative treatment to date and local recurrences remain frequent. Surgeons need new tools to maximize benefit from surgery. The aim of this project was the development and validation of antibodies (Ab) for fluorescence guided surgery. The systematic amplification of MDM2 in this subgroup of tumors results in a metabolic signature related to serine metabolism. We showed that MDM2 is recruited to chromatin to regulate a transcriptional program involving amino acid metabolism and particularly to the serine synthesis pathway enzymes and its transmembrane transporter (SLC)-1A4.

We confirmed that the serine carrier SLC1A4 is overexpressed in LPS cell lines and on fresh patient's tumors in LPS-WD and -DD. Using Phage display technology, we developed six antibodies against the extra membrane loop domain of the SLC. We validated four Antibodies in western blot, QPCR, FACS and immunofluorescence microscopy using cell lines with or without expression of SLC1A4 and LPS cell lines with Sh-SLC1A4. We confirmed the same tropism in immunohistochemistry on human kidney, testicular and skin samples as the commercial antibody targeting the intracellular part of the transporter. We started testing them for diagnosis on several LPS with promising results. We also confirmed their specificity on mice tissue samples, that allow us to test human form of the antibodies in PDX LPS models. In a collaborative study with SurgiMab, we managed to show intense fluorescent signal in the tumor after peritoneal injection with no secondary effect on mice.

In conclusion, in vitro and in vivo experiments are very encouraging for "fluorescence guided surgery" in LPS-WD and LPS-DD and have to be tested on human in a clinical trial after conducting a study on the pharmacodynamics, pharmacokinetics and toxicity.

68Ga DOTATOC PET-CT and 123I-mIBG scan discordances in a refractory case of pediatric neuroblastoma: tumor heterogeneity with implications for patient management

Adrien LATGE[1], Sèverine BRILLOUET[2], Laurent GUILLON[1,2], Marion GAMBART[3], Krim MEHDI AHMED[1], Delphine VALLOT[1], Frederic COURBON[1,2], Lavinia VIJA[1,2]

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[2] Centre de Recherche en Cancérologie de Toulouse

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High-risk refractory neuroblastomas carry poor overall survival, and novel approaches must be explored in order to improve global outcome. Meta-iodobenzylguanidine (mIBG) has been used to evaluate disease extent when coupled with iodine-123 due to the high expression of noradrenaline transporter (NAT) in neuroblastoma cells. In recent years, 68Ga-DOTATOC has emerged as a new PET-CT tool to screen for somatostatin receptor subtype 2 (SSTR-2) overexpression, opening the way to internal radiotherapy mediated by 177Lu-DOTATATE.

Aim: We compared the differential biodistribution of these two imaging biomarkers in a 6 year old patient with bone metastatic left adrenal neuroblastoma undergoing assessment for eligibility for molecular radiotherapy with Iodine-131 MIBG or Lu-177 DOTATATE as this patient progressed on bone metastases after three lines of chemotherapy and local irradiation of a lesion of the vertex.

Material and methods: I-123 MIBG scintigraphy was performed with both planar and SPECT/CT of the whole body at 24 h post injection. Ga-68 DOTATATE PET CT was performed on a Discovery Omni Legend PET/CT system according to BMI and pediatric guidelines.

Results: Dual exploration with 123I-mIBG scintigraphy and 68Ga-DOTATOC PET-CT was performed to evaluate the more appropriate therapeutic strategy. We observed significant mismatch regarding bone lesions, some overexpressing NAT and/or SSTR-2.

Conclusion: This rare presentation highlights the phenotypic heterogeneity of metastases after various lines of chemotherapy. With more than half of lesions with no or weak SSTR-2 expression, 177Lu-DOTATATE internal therapy was ruled out. Further investigations are needed to better comprehend this tumor mismatch and its prognostic implications. Screening of molecular targets using

complementary nuclear imaging techniques is an interesting option to guide treatment of refractory neuroblastomas.

Expansion of TREM1+ regulatory myeloid cells in steatohepatitis-HCC associates with poor prognosis and resistance to immune checkpoint blockade

Julie GIRAUD[1], Domitille CHALOPIN-FILLOT[1,2], Eloïse RAMEL[1], Thomas BOYER[1], Marie-Alix DERIEPPE[3], Atika ZOUINE[4], Jean-Frédéric BLANC[5], Laurence CHICHE[5], Christophe LAURENT[5], Macha NIKOLSKI[2], Maya SALEH[1]

[1] IMMUNOLOGY from CONCEPT and EXPERIMENTS to TRANSLATION

[2] Institut de Biochimie et Génétique Cellulaires

[3] University of Bordeaux Animal facilities, 33600 Pessac, France

[4] Bordeaux University, CNRS UMS3427, INSERM US05, Flow Cytometry Facility, 14 TransBioMed Core, 33000 Bordeaux, France

[5] University of Bordeaux Hospital, Division of Gastrohepatology and Oncology, Haut Leveque Hospital, 33604 Pessac, France

Hepatocellular carcinoma (HCC) is an inflammation-associated cancer arising from viral and non-viral etiologies. Expansion of suppressive myeloid cells is a hallmark of chronic inflammation and cancer, but their heterogeneity in HCC is not fully resolved and might underlie immunotherapy resistance in the steatohepatitis setting. Here, we present a high resolution atlas of hepatic innate immune cells from patients with HCC that unravels a steatohepatitis contexture characterized by influx of inflammatory and immunosuppressive myeloid cells. A discrete myeloid cell population identified by selective expression of TREM1 and CD163 expands in steatohepatitis-HCC. We refer to this population as TREM1+ regulatory myeloid cells (Mreg), as it potently suppresses T cell effector functions, highly expresses TGFB1 and IL13RA1 and localizes to HCC fibrotic lesions. Deconvolution analyses in large cohorts of patients with HCC and other solid tumors reveals that the density of TREM1+ Mreg increases in advanced cancer stages, associates with poor prognosis, and therapeutic resistance to PD-1 blockade. Experimentally, TREM1 engagement potentiates T cell suppression, and its inhibition improves anti-tumor immunity and HCC tumor eradication. Our data identify a steatohepatitis-HCC immunosuppressive tumor microenvironment and support myeloid subset-targeted immunotherapies to treat HCC.

T-cell exhaustion is an independent predictive biomarker of clinical outcome in high grade serous ovarian cancer regardless of homologous recombination deficiency status

Clara Maria SCARLATA[1,2], Anna SALVIONI[1,2], Mathilde DEL[1], Marie MICHELAS[1,2], Pierre VUATTOUX[1], Noémie THEBAULT[1,2], Carlos MARTINEZ-GOMEZ[1], Nathalie VAN ACKER[1], François-Xavier FRENOIS[1], Christine TOULAS[1,2], Guillame BATAILLON[1], Jean-Pierre DELORD[1,2], Alejandra MARTINEZ[1,2], Maha AYYOUB[1,2]

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High-grade serous carcinoma (HGSC) is the most frequent subtype of epithelial ovarian cancer. Approximately 50% of cases are homologous recombination deficient (HRD). PARP inhibitors have significantly improved the prognosis of patients with HRD tumors, but the clinical outcome is still poor. Despite the immunogenic nature of HGSC, the disease exhibits low response rates to immune checkpoint blockade (ICB) monotherapy in advanced line settings. We have previously identified, in epithelial malignancies including HGSC, CD4 and CD8 populations of tumor-infiltrating and antigen-specific T cells that display features of terminal exhaustion. These populations were key players in the response to anti-PD-1 in patients with epithelial tumors.

Here, we set out to characterize tumor-infiltrating T cells in a cohort of 80 HGSC patients treated at our institution from whom we collected tumor samples prior to therapy in which HRD status was assessed. Infiltration and exhaustion of CD4 and CD8 were assessed by multiplex immunofluorescence and multiparametric flow cytometry. Immunofluorescence analysis showed no difference in CD8 or CD4 T cells infiltration between HRD and homologous recombination proficient (HRP) tumors. Instead flow cytometry analysis showed an increased frequency of terminally exhausted PD-1HighTIM-3+ CD8 T cells and terminally exhausted PD-1HighTIM-3+CD39+ CD4 T cells in HRD tumors. Univariable analyses showed exhaustion parameters to be significant predictors of progression-free survival (PFS). The frequencies of exhausted CD4 and CD8 T cells stood out as predictors of PFS in multivariable analyses.

Altogether, these results provide the first evidence of a link between T-cell exhaustion and HRD status and reveal T-cell exhaustion as an independent predictor of disease outcome. They also underline the major role played by the antitumor immune response in HGSC and warrant the development of combination immunotherapies despite the lack response to ICB monotherapy.

Metabolic networks regulated by Mut-p53: an integrated approach to design new therapeutic strategies

Oriana VILLAFRAZ[1], Pierre-François ROUX[1], Carlo DE BLASIO[1], Hanna KULYK BARBIER[2,3], Matthieu LACROIX[1], Jean-Charles PORTAIS[2,3,4], Laurent LE CAM[1]

[1] Institut de Recherche en Cancérologie de Montpellier

[2] Toulouse Biotechnology Institute, Bio & Chemical Engineering

[3] MetaToul-MetaboHUB

[4] RESTORE research lab

P53 is a major tumor suppressor as highlighted by the high prevalence of somatic p53 mutations in many cancer types and the strong predisposition to multiple early-onset cancers in Li-Fraumeni Syndrome (LFS) patients that carry germline p53 mutations. We have generated datasets related to the metabolic functions of 2 clinically relevant hot-spot Mut-p53 (R248W and R175H) commonly found in human cancers. We profiled mouse embryonic fibroblasts (MEFs) harboring conditional knock-in (cKI) alleles (R245W or R172H) only or in combination with the Mdm2, Mdm4 or E4f1 cKO alleles in order to identify previously unknown mutp53-specific metabolic networks and functions of the upstream regulators of the p53 pathway in their regulation.

Our analyses of p53-deficient MEFs pointed at a previously unknown implication of p53 in the transsulfuration pathway and in taurine metabolism. Briefly, we found that p53 inactivation, as well as expression of the p53R245W or the p53R172H mutants, impair the induction of Cystathionine b-synthase (CBS) by the DNA-damaging agent doxorubicin and reduces mRNA levels of Fmo2, Fmo3, Fmo4, and Fmo6 which are associated to antioxidant functions. Our data suggest that p53 plays a pivotal role in the complex metabolic network composed of serine/glycine metabolism, transsulfuration pathway and taurine metabolism to maintain a balanced redox state.

In addition to our in vitro models, we aim to develop new Li-Fraumeni Syndrome mouse models with inducible loss of heterozygosity (LOH) and to determine the effects of timing LOH on the tumor spectrum and survival in animals harboring mutant p53R172H or p53R245W, two of the top mutated sites in LFS patients.

We are willing to address important unsolved questions in the cancer field related to the metabolic functions of Mut-p53 and the role of regulators of the p53 pathway.

LIST OF POSTER PRESENTATIONS

P01 - PDL-1 antibody fragment expressed on the cell surface of Toxoplasma gondii enhances anti-tumoral efficacy. Muna ALJIELI, *ISP, University of Tours, INRAE*

P02 - INFERRING MORPHOLOGICAL PATTERNS OF EGFR GENE MUTATION FROM LUNG CANCER TISSUES USING LARGE SCALE ARCHITECTURES. Nisma AMJAD, *Ummon HealthTech*

P03 - Identification of novel selective HDAC6 inhibitor against triple negative breast cancer. Ivana BELLO, *Department of Pharmacy (DoE 2023-27), School of Medicine and Surgery, University of Naples "Federico II", Via Domenico Montesano, 80131, Naples, Italy*

P04 - Monte Carlo modeling of multileaf collimator of an helical tomotherapy using GATE. Sheraz BLAS, Centre de Recherche en Cancérologie de Toulouse - Université Toulouse 3 Paul Sabatier

P05 - Role of PUFA - GPCR Signaling in Heterotypic Cell Communication in Liver Cancer. Tommy CHASTEL, *Institut de Recherche en Cancérologie de Montpellier*

P06 - Deciphering cellular interactions through gene regulatory network inference. Hugo CHENEL, *Centre de Recherche en Cancérologie de Toulouse*

P07 - Diagnostic radiolabelled silica nanoparticles as an EPR effect guided nanoplatform. Maelle DELEUZIERE, *Synthèse et physico-chimie de molécules d'intérêt biologique, Laboratoire de chimie de coordination, ToNIC*

P08 - FGF19 and its analog Aldafermin cooperate with MYC to induce aggressive hepatocarcinogenesis. Guillaume DESANDRE, *Institut de Génétique Moléculaire Montpellier*

P09 - CLL B cells are able to acquire functional Folate Receptor β (FRβ) from Nurse-like cells by trogocytosis, which is associated with their activation status. Marcin DOMAGALA, *Centre de Recherche en Cancérologie de Toulouse*

P10 - Exploiting Transcription-Replication Conflicts As a Novel Therapeutic Intervention in Multiple Myeloma. Laure DUTRIEUX, *Institut de Génétique Humain*

P11 - Tools for analysing spatial data in the context of immuno-oncology. Abdel Mounim ESSABBAR, *Centre de Recherche en Cancérologie de Toulouse*

P12 - New function(s) of chk1 kinase in the autophagy process. Lucie FABRIZI, *Centre de Recherche en Cancérologie de Toulouse - Université Toulouse 3 Paul Sabatier*

P013 - Long pentraxin-3 as a tumor promoter in medulloblastoma. Serena FILIBERTI, *Laboratorio di Oncologia e immunologia sperimentale-Dipartimento di Medicina Molecolare e Traslazionale-Università degli Studi di Brescia*

P14 - Development of conformational and tissue specific antibody against a GPCR as potential drug candidate in immuno-oncology. Lisa FRELAT, *G.CLIPS Biotech*

P15 - Revolutionizing Cancer Immunotherapy: Nanotechnology Unleashes Ferroptosis for Targeted Precision. Masoud GHANAATIAN, *Master 1 Bio-santé - parcours Toulouse Graduate School of Cancer, Ageing and Rejuvenation (CARe)*

P16 - Interest of circulating cell-free DNA fragmentation as biomarker in pancreatic cancer. Sophie GILBERT, *Centre de Recherche en Cancérologie de Toulouse - Adelis*

P17 - Crosstalk between the modulation of EZH2 functions, lipid metabolism and stemness in diffuse intrinsic pontine glioma. Guillaume HERRAULT, *U1312 - MIRCADE team, Université de Bordeaux*

P18 - Links between pyruvate metabolism and translation in melanoma. Morane HOUDEVILLE, *Institut de Recherche en Cancérologie de Montpellier - INSERM, U1194, Montpellier F-34298, France*

P19 - Transcriptional regulatory networks unravel cell states from immune cell type deconvolution and uncovers cell niches predictive of cancer progression. Marcelo HURTADO, *Centre de Recherche en Cancérologie de Toulouse*

P20 - Transcriptomic Profiling of the Non-Small Cell Lung Cancer (NSCLC) Microenvironment Identifies a Duality in Natural Killer Cell Behavior. Leila KHAJAVI, *Centre de Recherche en Cancérologie de Toulouse*

P21 - Do mechanical forces induce a protumoral dialogue between the tumor and the adjacent healthy tissue? Claire LAC, *Centre de Recherche en Cancérologie de Toulouse*

P22 - Unravelling the role of early dissemination in colorectal cancer, validation in patients. Tinhinan LAHLOU, *Institut de Génomique Fonctionnelle*

P23 - Translation meets cytokine exchanges: the translatomic implication of IFNg and IDO1 in a novel subtype of pancreatic ductal adenocarcinoma. Mehdi LIAUZUN, *Centre de Recherche en Cancérologie de Toulouse*

P24 - Dissecting cellular communication in the tumour micro-environment through gene regulatory network inference. Malvina MARKU, *Centre de Recherches en Cancérologie de Toulouse*

P25 - Function of USP7 in normal hematopoiesis. Antoine NOUHAUD, *Centre de Recherche en Cancérologie de Toulouse*

P26 - Identification of long non-coding RNAs involved in Acute Myeloid Leukemia chemoresistance. Romain PFEIFER, *Centre de Recherche en Cancérologie de Toulouse*

P27 - polyMORPHOS | SOURIS - XGBoost Forest Algorithm Combined with Flux Balance Analysis Predicts Survival Outcome and Elucidates Unforeseen Metabolic Vulnerabilities in Acute Myeloid Leukemia Patients. Nathaniel POLLEY, *Centre de Recherche en Cancérologie de Toulouse*

P28 - Circulating neoantigen-specific CD8 T-cell responses: a biomarker of response to immune checkpoint blockade in lung and bladder cancers. Célia RAMADE, *Centre de Recherches en Cancérologie de Toulouse, Inserm, CNRS, Université Toulouse III-Paul Sabatier, Université de Toulouse, Toulouse, France - IUCT-Oncopole, Toulouse, France*

P29 - Acquired chemoresistance in pancreatic adenocarcinoma: mechanism implicating the stromal transcription factor Zbtb16 ? Ludmila RECOULES, *Centre de Recherche en Cancérologie de Toulouse*

P30 - Impact of DDR1 on Renal Cell Carcinoma development. Chloé REDOUTÉ TIMONNIER, *BoRdeaux Institute of Oncology*

P31 - Multiple myeloma is associated with dysregulation of BCL6-expressing T cells frequency and function. Thomas RICHARME, *Centre de Recherche en Cancérologie de Toulouse, team GENIM*

P32 - Cancer cells transfer invasive properties through collagen-tracks. Lucile ROUYER, *University of Bordeaux, Inserm, UMR1312, BRIC, BoRdeaux Institute of onCology, 146 Rue Léo Saignat, Bordeaux, F-33076, France*

P33 - Differences in antigen-specific CD8 and CD4 T-cell responses according to primary tumor site in human papillomavirus-induced epithelial cancers. Victor SARRADIN, *IUCT Oncopole - Centre de Recherche en Cancérologie de Toulouse*

P34 - Inflammation-induced epithelial plasticity can be by-passed through Vps34 inactivation to limit pancreatic cancer initiation. Hala SHALHOUB, *SigDYN - Toulouse Cancer Research Center*

P35 - A Comprehensive Study of a Pancreatic Cancer Subtype: The Interplay between Translation and Transcription in the Tumor Microenvironment. Jacobo SOLORZANO, *Centre de Recherche en Cancérologie de Toulouse*

P36 - Adapted Physical Activity for Children treated for Cancer and Insulin Sensitivity. Justine THOMAS, *Institut des Maladies Métaboliques et Cardiovasculaires*

P37 - Role of the Striatin3 protein in liver cancers. Camille TOCQUEVILLE, *BoRdeaux Institute of Oncology - Université de Bordeaux - Sciences de la santé / Sciences de l'Homme (Carreire / Victoire)*

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