1st ONCOLille days

November 2-4, 2022
Huriez Hospital –Research Campus
Amphitheater Lyderic, UFR3S
Lille, France

ONCOLille
LILLE CANCER RESEARCH INSTITUTE

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Welcome from the director of ONCOLille

Dear Congress Participants,

Welcome to the 1st ONCOLille Days!

The ONCOLille institute is the latest Cancer Research Institute born in France. Its inauguration took place on the 12th of October 2022 and launched a new research dynamic dedicated to cancers.
ONCOLille singularity is that it gathers, in one building, biologists, chemists, physicists, mathematicians, psychologists, in social and human sciences, health economists and clinicians and state-of-the-art technical plateaux (BioMEMS, laser laboratory, organoids/tumoroids, metabolism, single cell, virology, infectiology…) to develop a fundamental, and pre-clinical interdisciplinary research of excellence on bad prognosis cancers and on the mechanisms of persistence, resistance to therapies and dormancy.

Being located in close contact to the two Lille hospitals treating cancer patients: the Lille hospital (CHU Lille) and the Regional Cancer Center (Centre Oscar Lambret), we will be keen on transferring our research results to the clinics for the patient benefit.
For the first edition of the ONCOLille Days meeting, we decided to keep this particularity of our institute, that is the interdisciplinarity, in the scientific program. For that, we propose 9 scientific sessions: Tumor Resistance & Plasticity, Molecular Mechanisms and Signaling, Cancer Targeted Therapy, AI & Computational Systems Biology of Cancer, Cancer Adaptation Metabolism, Mathematical Modelling for Cancer Research, Technologies for Health in Cancer, Cancer & Labour Force, Interventional Research in Cancer.

13 international speakers, all experts in these fields will introduce the scientific sessions. We deeply thank them for accepting our invitation. For our plenary lecture, we are very proud and honoured to welcome Dr Douglas Hanahan of Lausanne (Switzerland) who described for the first time in his famous review “The Hallmarks of Cancer”, the characteristics of Cancers and then in the following updated reviews “Hallmarks of Cancer: The Next Generation” and “Hallmarks of Cancer: New Dimensions”, the importance of the tumor microenvironment, tumor plasticity and heterogeneity in cancer progression/behaviour and in developing new therapeutic approaches.
We wish you a very nice stay in our beautiful historic city of Lille and hope you will enjoy the scientific program and also our gala reception that will take place in the second French Museum of Arts after “Le Louvre” Museum in Paris, that is the Lille Museum of Fine Arts, that you will be able to visit during the diner.

Dr Isabelle VAN SEUNINGEN
Director of ONCOLille institute

Practical information

Internet connection details

To connect on internet, please use EDUROAM if you've an account.
Otherwise, you may connect on the network ULILLE-ACCUEIL using the following details

login: CG-6350
Password: c3FnbPGd6q

Lunches and coffee breaks

Lunch and coffee breaks will be provided in the lobby of the conference building

Social Events

Wednesday November 2

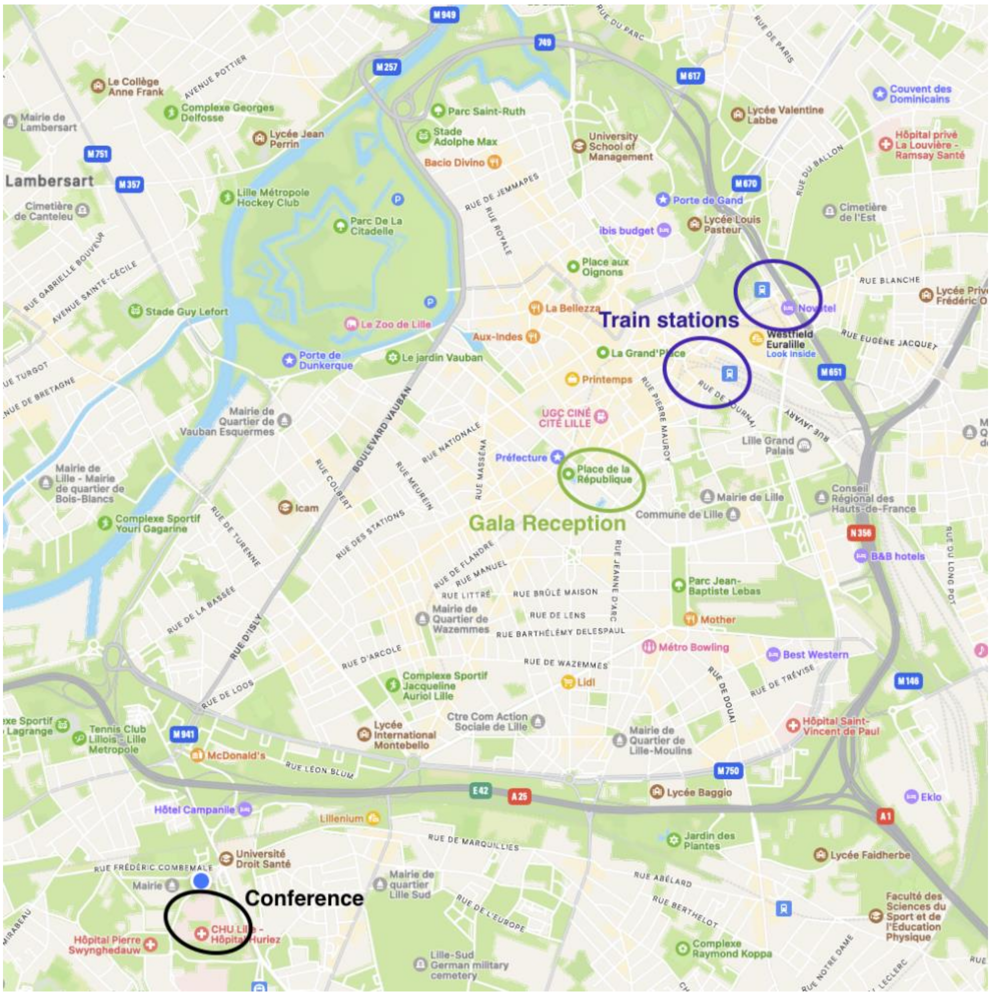
5.30-7.0 pm: Poster session with wine and beer
Location: Conference Building

Thursday November 3

7 pm: Visit of the Museum Palais des Beaux-Arts de Lille followed by a Gala Reception (8.30 pm) at the same place.

Location: Place de la République (next to the Metro station République Beaux Arts - Line 1)

Map of Lille



Train stations
Gala Reception
Conference
Place de la République
Lambersart
Parc De La Citadelle
Le Zoo de Lille
Porte de Dunkerque
Le jardin Vauban
Porte de Gand
Place aux Oignons
La Grand'Place
Printemps
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Lillenium
Hôtel Campanile
Université Droit Santé
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Hôpital Pierre Swynghedauw
Lille-Sud German military cemetery
Complexe Raymond Koppa
Faculté des Sciences du Sport et de l'Education Physique
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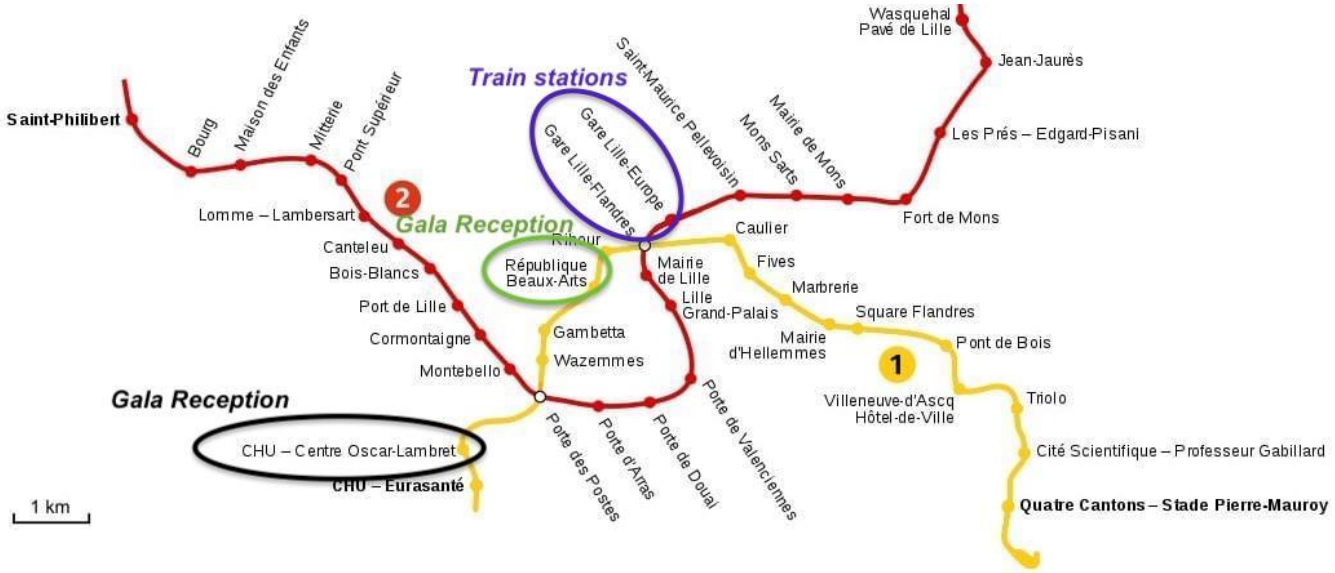
RUE DE MARQUILLIES

Lille Subway stops



Gare Lille-Europe

Gare Lille-Flandre

Gala Reception
Palais des beaux Arts

Conference
Faculté de médecine
de Lille
- Pôle Recherche-

Wednesday, november 2nd

9.00-10.00 am Registration - Coffee

10.00-10.30 am Welcome

Isabelle VAN SEUNINGEN, Director of ONCOLille Institute

10.30-12.00 pm Symposium 1: Tumor Resistance & Plasticity

Chairs: Chann Lagadec & Loic Lemonnier

Gergely SZAKACS (Vienna, Austria)
Targeting multidrug resistant cancer- an unfinished business

Mathilde BRULE (Lille, France)
Development of tools for spatio-temporal analysis of phenotypic dynamics of breast cancer cells.

Julien CICERO (Lille, France)
Neurotrophins promotes brain metastasis of triple negative breast cancer through Src kinase family activation

Lunch (Stands/commercial/companies' presentations)

1.30-2.00 pm **Presentation Polyplus® previously E-Zyvec**

2.00-3.30 pm Symposium 2: Molecular Mechanisms and Signaling

Chairs: Dimitra Gkika & Albin Pourtier

Marco DEMARIA (Groningen, the Netherlands)
Modulation of senescence-associated mechanisms in cancer therapy

Clara LEWUILLON (Lille, France)
Deciphering the PD-1/PD-L1 calcium signature in the immunological synapse: microfluidic single cell technology towards precision immunotherapies

Julie AUWERCX (Amiens, France)
In Vitro Study of the Role of TRPM7 Kinase in Metastatic Mechanisms of Pancreatic Cancer Cells

Coffee break

4.00 pm Plenary Lecture

Douglas HANAHAN (Lausanne, Switzerland)
Hallmarks of Cancer-further considered, and new insights into the immuno-suppressive tumor microenvironment

5.30-7.30 pm Poster session and social gathering

Thursday, november 3rd

8.30-10.30 am Symposium 3: Cancer Targeted therapy
Chairs: Olivier Morales & Salomon Manier

Celso REIS (Porto, Portugal)
Altered glycosylation in cancer: dissecting the molecular mechanisms and understanding the clinical implications

Hervé WATIER (Tours, France)
In search of the best antibody format for immune checkpoint inhibitors

Silvia GAGGERO (Lille, France)
IL-2 is inactivated by the acidic pH environment of tumors enabling engineering of a pH-selective mutein

Camille TRIOEN (Lille, France)
Role of Galectin-9 in the Induction of Tolerogenic Dendritic Cells Mediated by Nasopharyngeal Carcinoma Exosomes

Coffee break

11.00-12.30 pm Symposium 4: AI & Computational Systems Biology of Cancer
Chairs: Mohamed Elati & Wajdi Dhifli

Vera PANCALDI (Toulouse, France)
Machine learning and multi-omics approaches for the description and modelling of the tumour microenvironment

Bahram AHMADIAN (Lille, France)
Classification of single cancer cells based on their biophysical signatures

Quentin REZARD (Lille, France)
High-throughput biophysical analysis of single cells

Lunch 1.30-2.00 pm **Presentation Polyplus® previously E-Zyvec**

2.00-3.30 pm Symposium 5: Cancer Adaptation Metabolism
Chairs: Laurent Mortier & Mathias Chamaillard

François GOLDWASSER (Cochin Institute, France)
Rest energetic assessment and sensitivity to immune checkpoint inhibitors in oncology

Dana SIMIUC (Lille, France)
Metabolic adaptation of breast cancer cells: variability of single cells responses

Nilmara DE OLIVIERA ALVES (Lille, France)
Bacterial colibactin-induced lipid accumulation and loss of a c-type lectin cooperates for supporting an immune-suppressive microenvironment in right-sided colon cancer

Coffee break

4.00-5.30 pm — Symposium 6: Mathematical Modeling for Cancer Research
Chairs: Sophie Dabo & Alexandre Poulain

Mahlet TADESSE (Georgetown U, USA)
Mixture models and variable selection to identify cancer subtypes and biomarkers

Charles ELBAR (Paris, France)
Pressure jump for the Cahn-Hilliard equation: an application to tumor growth

Emma LESCHIERA (Paris, France)
A mathematical model to study the impact of intra-tumour heterogeneity on anti-tumour CD8+ T cell immune response

7.00 pm — Museum visit Palais des Beaux-Arts de Lille
8.30 pm — Gala Reception (Palais des Beaux-Arts de Lille)

Friday, november 4th

8.30-10.00 am — Symposium 7: Economic consequences of cancer and related Public Policies
Chairs : Nicolas Debarsy & Christine Le Clainche

Cathy BRADLEY (Colorado School of Public Health, USA)
Cancer's financial impact

Nicolas DEBARSY (Lille, France)
Impact of early diagnostic on oesogastric cancer survival

Sophie MASSIN (Lille, France)
Willingness to pay or to make a gift as a measure of efficacy of novel cigarette plain pack warnings: a randomized controlled experiment

Coffee break

10.30-12.30 pm Symposium 8: Technologies for Health in Cancer
Chairs: Nadira Delhem & Vincent Senez

Shuichi TAKAYAMA (GeorgiaTech, USA)
High-Throughput 3D Cellular Cancer Models

Petteri UUSIMAA (Modulight, Fl)
Cloud connected medical devices for photoactivated drug delivery

Laurine ZIANE (Lille, France)
Development of a light emitting device for the treatment of peritoneal carcinomatosis of ovarian origin by intracavitary photodynamic therapy

Lucas ROUSSEL (Lille, France)
Spidermass: a novel tool for immune score for patient prognosis in ovarian cancer

Lunch (Stands/commercial/companies' presentations)

1.30-2.00 pm **Presentation Bio-Techne**

2.00-4.00 pm Symposium 9: Interventional Research in Cancer
Chairs: Delphine Grynberg & Christelle Duprez

Serge SULTAN (Montréal, Canada)
Why (and how) we should care about Quality of Life in childhood cancer

Kristopher LAMORE (Lille, France)
Digital health interventions to support cancer patients and caregivers: what works? For whom? An umbrella review

Pauline WAROQUIER (Brussels, Belgium)
Improving emotion regulation in breast cancer patients in the early survivorship period: Efficacy of a brief ecologically boosted group intervention

Pauline JUSTIN (Lille, France)
Raising the physicians' awareness regarding Young Carers in oncology: an interventional research

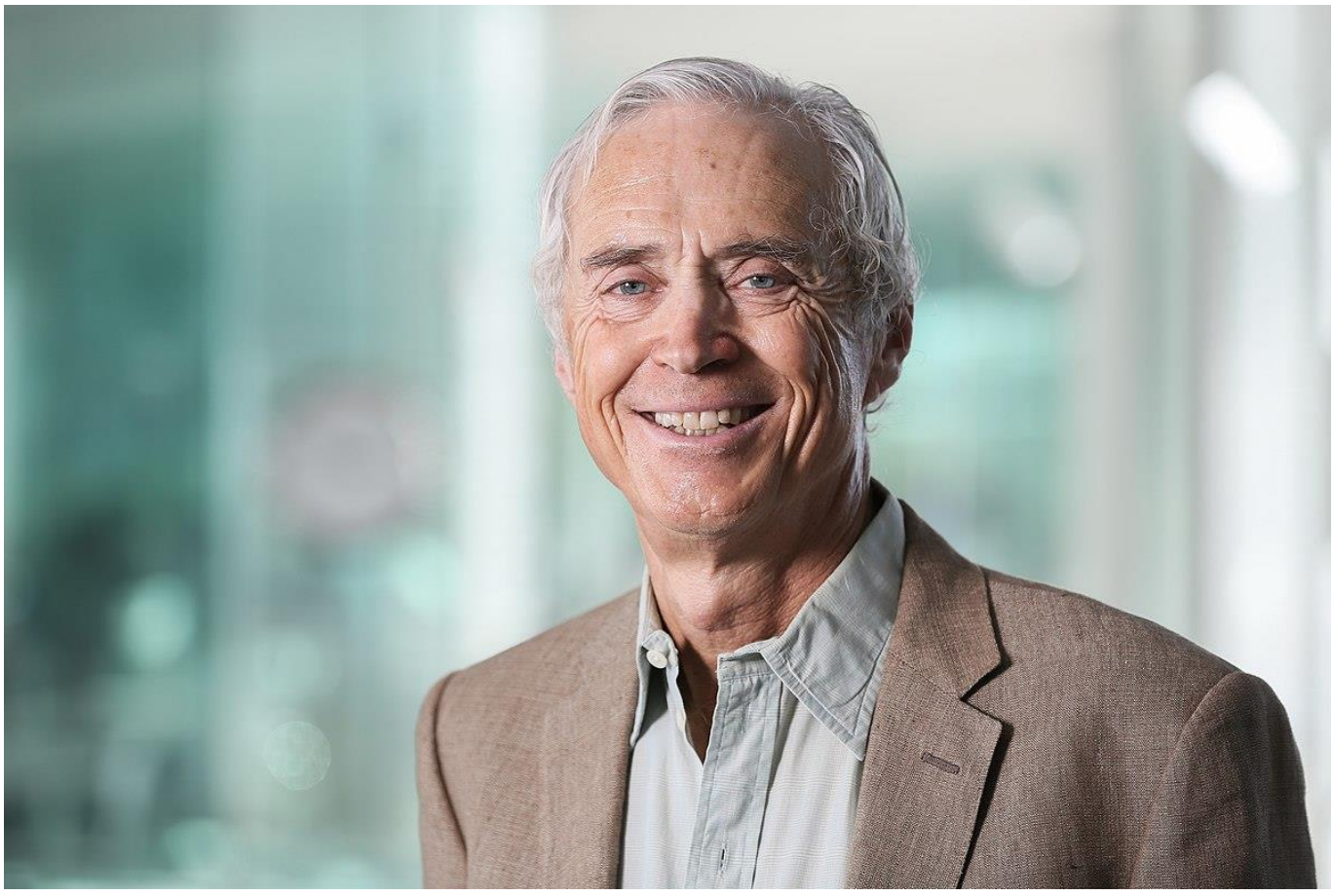
4.00-5.00 pm Poster and selected speakers' prizes
Closure and Departure

Plenary Lecture

Hallmarks of Cancer-further considered, and new insights into the immuno-suppressive tumor microenvironment

Douglas HANAHAN

[1]*Professor of Molecular Oncology, and former director of the Swiss Institute for Experimental Cancer Research at EPFL*
[2]*Distinguished Scholar, Ludwig Institute for Cancer Research, Lausanne Branch SW*



Abstracts

O1 - Targeting multidrug resistant cancer- an unfinished business

Gergely SZAKACS

[1]*Institute of Enzymology, Research Centre for Natural Sciences, 1117 Budapest, Hungary.*
[2]*National Laboratory for Drug Research and Development, 1117 Budapest, Hungary.*

Clinical evidence shows that, following initial response to treatment, drug-resistant cancer cells frequently evolve, and eventually most tumors become resistant to all available therapies. The most straightforward cause of therapy resistance is linked to cellular alterations that prevent drugs to act on their target. Upregulation of cell membrane efflux transporters of the ATP-binding cassette (ABC) superfamily leads to simultaneous resistance against structurally and functionally unrelated chemotherapeutic agents. In particular, P-glycoprotein (Pgp, MDR1) was shown to be expressed in several drug resistant malignancies. Based on the correlation of P-glycoprotein expression and function with unfavorable treatment response, it is universally accepted that pharmacological modulation of the MDR phenotype has the potential to significantly increase the efficacy of currently available anticancer therapies. Unfortunately, despite a few early successes, clinical trials conducted with Pgp inhibitors did not fulfill this expectation, failing to confirm clinical benefit. Failure of the trials led to a setback in research, and the shutdown of the pharmaceutical development of transporter inhibitors for the improvement of anticancer therapy. Yet the "transporter problem" has not vanished, as evidenced by new studies supporting the relevance and benefit of research on the role of ABC transporters in clinical drug resistance. Failure of the inhibitors has boosted research in other directions, exploring the possibility to evade efflux, or to exploit the paradoxical sensitivity associated with efflux-based drug resistance mechanisms. In this talk I will describe new approaches to combating multidrug-resistant cancer, including the development of drugs that engage, evade or exploit efflux by P-glycoprotein.

O2 - Neurotrophins promotes brain metastasis of triple negative breast cancer through Src kinase family activation

Julien Cicero[1,2,3], Sarah Trouvilliez[1,3], Martine Palma[1,3], Gaetan Ternier[4], Laurine Decoster[4], Nicolas Barrois[5], Lucie Dehouck[2], Eloise Happernegg[1,2,3], Roland Bourette[1], Eric Adriaenssens[1], Chann Lagadec[1,3], Cagatay Mehmet Tarhan[6,7], Dominique Collard[7,8], Zied Souguir[9], Elodie Vandenhaute[9], Grégory Maubon[9], Nathalie Maubon[9], François Sipieter[10], Nicolas Borghi[10], Paolo Giacobini[4], Vincent Prevost[4], Fabien Gosselet[2], Xuefen Le Bourhis[1], Isabelle Van Seuningen[1], Caroline Mysiorek[#] and Robert-Alain Toillon[1,3].

[1]Univ. Lille, CNRS, Inserm, CHU Lille, UMR9020-U1277 - CANTHER - Cancer Heterogeneity Plasticity and Resistance to Therapies, F-59000 Lille, France
[2]Univ. Artois, UR 2465, Laboratoire de la Barrière Hémato-Encéphalique (LBHE), F-62300 Lens, France 3GdR2082 APPICOM- « Approche intégrative pour une compréhension multi-échelles de la fonction des protéines membranaires ».
[4]Univ. Lille, Inserm, CHU Lille, Équipe développement et plasticité du cerveau neuroendocrine, FHU 1 000 jours pour la Santé, Lille Neuroscience et Cognition, UMR-S1172, 1 place de Verdun, 59045 Lille Cedex, France.
[5]Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, US 41 – UAR 2014 – PLBS, F-59000 Lille, France
[6]Univ. Lille, CNRS, Centrale Lille, Junia, Univ. Polytechnique Hauts-de-France, UMR 8520 -IEMN -Institut d'Electronique de Microélectronique et de Nanotechnologie, F-59000 Lille, France
[7]LIMMS/CNRS-IIS IRL2820, The University of Tokyo, Tokyo, Japan
[8]CNRS, IIS, COL, Univ. Lille SMMiL-E project, Lille, France
[9]HCS Pharma, F-59120 Loos, France
[10]Université de Paris, Centre National de la Recherche Scientifique (CNRS), Institut Jacques Monod, 15 rue Hélène Brion, 75013 Paris, France.

With nearly 2.3 million cases diagnosed worldwide each year and an estimated 685 000 deaths by 2020, breast cancer is the leading cause of cancer-related death in women. Brain metastases cause severe cognitive complications that severely impair quality of life. In TN breast cancer, the prognosis for brain metastases is particularly poor with a median survival of no more than 6 months. It is therefore crucial to know the molecular actors that promote the metastatic dissemination of triple negative breast cancer to the brain but also to prevent the proliferation of brain micrometastases that can cause fatal recurrences.

In order to recapitulate several final stages of brain metastasis, we used both human Blood- Brain-Barrier *in vitro* model, human organotypic 3D extracellular *in vitro* matrix, mice brain slices organotypic *ex vivo* culture and *in vivo* mice xenograft. These models are coupled with single cell, 3D and real time imaging techniques, including FRET biosensing. This unique experimental approach allows us to study the involvement of signaling pathways in these different biological processes. Using this innovative method, we have identified that inhibition neurotrophins receptor leads to a decrease in the activity of the underlying signaling pathways and consequently to a decrease in the ability of breast cancer cells to pass through the BBB, to grow and to colonize the brain parenchyma.

O3 - Development of tools for spatio-temporal analysis of phenotypic dynamics of breast cancer cells.

Mathilde Brulé[1] ; Marie Denoulet[1] ; Anaïs Horochowska[1]; Flavie Woesteland[1]; Xuefen LeBourhis[1]; François Anquez[2] and Chann Lagadec[1]

[1]Univ. Lille, CNRS, Inserm, CHU Lille, Centre Oscar Lambret, UMR9020 – UMR1277 - Canther – Cancer Heterogeneity, Plasticity and Resistance to Therapies, F-59000 Lille, France
[2]Univ. Lille, CNRS, UMR 8523 - PhLAM - Physique des Lasers Atomes et Molécules, F-59000 Lille, France

Cancer Stem Cells (CSCs) are particularly resistant to chemotherapy and radiotherapy. A relative phenotypic plasticity has been observed in some non- cancer stem cells (non-CSCs) able to reacquire a CSC phenotype under the effect of these treatments. The laboratory has recently discovered that non-CSCs reprogramming into CSCs involves inflammatory cytokines activating, through unknown pathway(s), Notch expression/downstream pathway and reacquisition of stem cell phenotype.

Conventional methods to study CSCs are limited to study dynamic and non- synchronized processes. To better understand this reprogramming and develop a strategy to prevent it, we have developed a protocol including a microscopy system and image analysis algorithms. Thus, individual cells can be followed through five days in several fluorescence channels in parallel.

To start with, the developed workflow were used to assess the spatio-temporal dynamic of stemness (pALDH1A1:mNeptune reporter), and redox state (Grx1- roGFP2). By fitting the fluorescence level curve of mNeptune, we could identify 3 populations of cells, CSCs, non-CSCs and stable intermediate cells. Using modified K(r) Ripley's function, we quantified that CSCs live in niches, CSC being closer to each other while excluding non-CSCs. Mainly phenotypically stable, a rare subpopulation of cells displays a dynamic phenotype with transitions from non-CSC to CSC, even with undisturbed conditions. Interestingly, it appears that those transitions could only occur within a specific environment.

All together, we developed a versatil tools to analyze phenotypic dynamic of process occurring through long period of time and/or asynchronously.

P1 - The role of senescence in the development of non- melanoma skin cancer in kidney transplant recipients : the impact of immunosuppressive drugs in vitro

Abi-Rached Henry[1,2] ; Bounaud Sophia[1]; Martin Nathalie[1]; Glowacki François[1,3], Mortier Laurent[2], Abbadie Corinne[1]

[1]*CANTHER - Univ. Lille, CNRS, Inserm, CHU de Lille, Batiment Oncolille – UMR9020- U1277*
[2]*Service de Dermatologie, Hôpital Claude Huriez, CHU de Lille.*
[3]*Service de Néphrologie, Hôpital Claude Huriez, CHU de Lille.*

Kidney transplant patients on immunosuppressive therapy (tacrolimus, azathioprine (6MP), and mycophenolate mofetil (MMF)) are 250 times more likely to develop squamous cell carcinomas (SCCs) than the general population. However, we observed an incidence drop when patients were switched to rapamycin. Tacrolimus, 6MP and MMF induce oxidative stress and DNA damage, both of which are known to promote senescence of epidermal keratinocytes. Our previous work showed that the senescence of these cells can favor neoplastic development in vitro. Moreover, it is established that most pre-neoplastic lesions contain many senescent cells. The hypothesis is therefore that tacrolimus, 6MP and MMF induce a premature senescence of keratinocytes that promotes the development of actinic keratosis that leads to cutaneous squamous cell carcinomas. Rapamycin has senolytic effects that could therefore carry a therapeutic effect on actinic keratosis. To test these hypotheses, we treated primary human keratinocytes (NHEKs) daily with tacrolimus, 6MP or MMF at concentrations close to patients' serum concentrations and monitored senescence markers. 6MP and MMF were toxic and did not influence senescence. On the contrary, tacrolimus induced senescence after 3 days, evidenced by an increase in cell size and granularity and a proliferation arrest. Secondly, we have shown that rapamycin has a toxic effect on NHEKs in spontaneous or tacrolimus-induced senescence. These preliminary results suggest that rapamycin and tacrolimus could shift the balance of senescent cells and therefore could directly influence keratinocyte cancer development. Moreover, the senolytic effect of rapamycin as a topical treatment for early-stage actinic keratosis could be interesting to investigate.

P2 - Role of the microenvironment on the resistance of leukemia cells to tyrosine kinase inhibitors, contribution of bioprinting

Mélanie Dhayer[1], Nicolas Germain[1], Salim Dekiouk[1], Philippe Marchetti[1]

[1]ONCOLille Cancer Institute - CANTHER « Cancer Heterogeneity, Plasticity and Resistance to Therapies » - UMR9020 CNRS – U1277 Inserm – Université de Lille – CHU de Lille - Team « Factors of persistence of leukemic cells »

Bone marrow provides a protective niche, allowing leukemic cells to survive until the subsequent acquisition of mutations responsible for tyrosine kinase inhibitors (TKI) resistance. Cells in this microenvironment, including stromal cells and adipocytes, interact with leukemia cells and influence their persistence and resistance to TKIs via fatty acid and/or mitochondrial transfer. Our aim is to bioprint a complex 3D model of bone marrow containing the cells surrounding leukemic cells, including adipocytes and stromal cells, in order to study the biology of leukemic cancer.

Firstly, we studied the influence of 3T3-L1 cells at different degrees of adipocyte differentiation in the presence of BCR-ABL, DA1-3B leukemia cells with different concentrations of TKI (Imatinib) in order to study their resistance. Leukemia cells become tolerant to Imatinib in the presence of differentiated pre-adipocyte 3T3-L1 cells and this resistance is proportional to the degree of adipocyte differentiation. Next, the same experiment was performed in bioprinted methacrylated gelatin hydrogels (GelMA). Once again, the presence of adipocytes promotes the tolerance of leukemic cells to TKIs.

A model of adipose spheroids has been bioprinted in GelMA, since this organization allows the preservation of stemness, differentiation in all mesenchymal lineages and an anti- inflammatory secretome closer to the tissue. The next step will be to obtain vascularized adipose spheroids which will be placed in the presence of ITK-treated leukemia cells to best mimic the tumor microenvironment of the bone marrow.

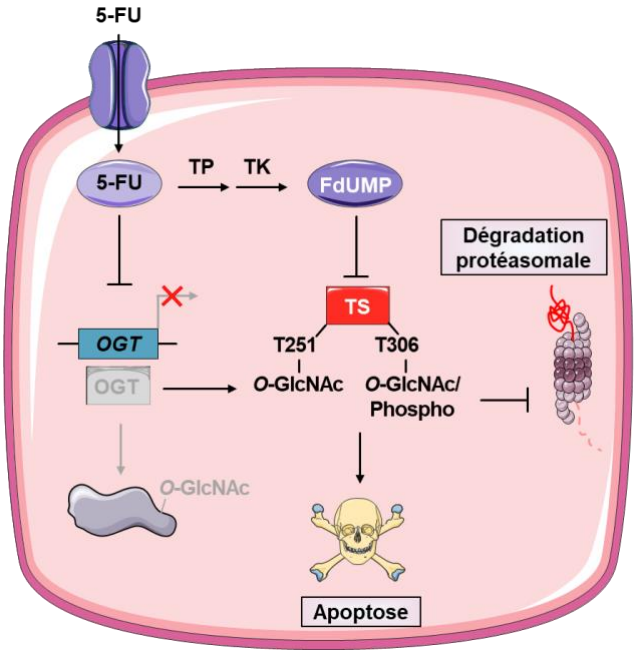
Key words : ITK, Leukemia, Adipocytes, Bioprinting, GelMA

P3 - O-GlcNAcylation of Thymidylate Synthase : a new regulatory mechanism of 5-Fluorouracil chemotherapy response in colorectal cancer

Ninon VERY, Stéphan HARDIVILLE, Tony LEFEBVRE, Ikram EL YAZIDI-BELKOURA

Unité de Glycobiologie Structurale et Fonctionnelle (UGSF), Univ. Lille, CNRS UMR 8576, France

Alteration of O-GlcNAcylation, a dynamic post-translational modification, is associated with tumorigenesis and tumor progression. Its role in chemotherapy response is poorly investigated. Standard treatment for colorectal cancer (CRC), 5-fluorouracil (5-FU), mainly targets Thymidylate Synthase (TS). TS O-GlcNAcylation was reported but not investigated yet. We hypothesize that O- GlcNAcylation interferes with 5-FU CRC sensitivity by regulating TS. We showed that OGT Interacts and modifies TS. We highlighted two major TS isoforms with 2 or 4 O-GlcNAcylated sites. TS-FdUMP complexed isoform and free TS isoform are predominantly O-GlcNAcylated respectively in 5-FU sensitive and resistant colon cancer cell lines. O-GlcNAcylation increases TS stability and OGT knock- down reduces 5-FU-induced apotosis of sensitive colon cancer cells. We reveal a crosstalk between O-GlcNAcylation and 5-FU metabolism that converges to 5-FU CRC sensitization by stabilizing TS. Overall, our data propose that combining 5-FU-based chemotherapy with Thiamet G could be a new way to enhance CRC response to 5 FU-based chemotherapies.



Keywords : O-GlcNAcylation, colorectal cancer, 5-FU therapy.

P4 - Development of a "metastasis-on-a-chip" to monitor cancer cells extravasation during metastatic process in breast cancer

Flavie WOESTELAND[1], Aude SIVERY[2], Marie DENOULET[1], Mathilde BRULE[1], Anaïs HOROCHOWSKA[1], Fabrice SONCIN[3,4], Xuefen LE BOURHIS[1], Anthony TREIZEBRE[2], Chann LAGADEC[1]

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[3]CNRS/IIS/Centre Oscar Lambret/Lille University SMMiL-E Project, CNRS Délégation Hauts-de-France
Univ. Tokyo CNRS UMI 2820, LIMMS, Tokyo, Japan
[4]CNRS IRL 2820; Laboratory for Integrated Micro Mechatronic Systems, Institute of Industrial Science, University of Tokyo

Introduction: With more than two million new cases diagnosed per year worldwide, breast cancer was, in 2020, the most diagnosed and deadliest cancer in women. 90% of breast cancer mortality is due to the formation of metastases that affect vital regions, mainly pulmonary, bone, cerebral and hepatic. Among the different subtypes of breast cancer, triple-negative has the worst prognosis with a high metastatic risk and a median survival that drops at 13 months when metastases develop. Faced with this major public health problem, it is essential to learn more about the mechanisms of metastasis and to characterize cancer cells capable of metastasizing to target them and limit this process.

Method: Our team has developed a microfluidic tool, a "metastasis-on-chip", with an innovative design that allow metastatic cancer cells tracking through an endothelial-like structure within a modulable environment, but more importantly extravasated cells can be collected for further characterization.

Results: We first established the design of the chip consisting of a double channel: the upper channel mimics the vascular structure while the lower channel collects extravasated cells. Then we were able to determine the conditions to obtain a complete, confluent and 3D endothelium in the upper channel. Finally, we were able to inject cells mimicking circulating cancer cells and follow the extravasation process until the cells passed through the collecting duct.

Conclusion: The innovative adaptative design of the chip combined with the microfluidic tool seem to make our model an interesting device to study metastasis *in vitro* under *more physiological* conditions.

P5 - Resistance of s-SHIP positive tumor cells in the MMTV- Wnt1 mouse model of breast cancer

Joséphine Louvieaux[1], Roland Bourette[1]

[1]*Univ. Lille, CNRS, Inserm, CHU Lille, Centre Oscar Lambret, UMR9020 – UMR1277 – Canther – Cancer Heterogeneity, Plasticity and Resistance to Therapies, F-59000 Lille, France*

Triple Negative Breast Cancer (TNBC) is the most lethal subtype of breast cancer. Despite the successes of emerging targeted therapies, relapse, recurrence and therapy failure rates in TNBC significantly outpace other subtypes of breast cancer. Mounting evidence suggests accumulation of therapy resistant Cancer Stem Cell (CSC) populations within TNBCs contributes to poor clinical outcomes. In order to investigate the nature of these resistant CSC, two transgenic mice models are combined to study these CSC : (i) the s-SHIP-GFP mice express green fluorescent protein (GFP) from the s-SHIP promoter. By using these mice, we have previously shown that s-SHIP/GFP is a marker of both normal and cancer stem cells of the mammary gland. (ii) The MMTV-Wnt-1 mice is a well-studied mouse model of multistep mammary tumorigenesis. We have generated bitransgenic mice by crossing these two models and obtained mammary tumors containing a subset of s-SHIP/GFP expressing cells. 3D cell cultures were established to investigate the drug resistance of these tumor cells. We obtained heterogeneous spheroids that reproduce tumor heterogenity with stromal, basal, and luminal cells, including a subset of s-SHIP/GFP positive cells. As a first approach, we investigated the effect of paclitaxel, a drug widely used in the treatment of breast cancer. We demonstrated that treatment with paclitaxel significantly increased the percentage of s-SHIP/GFP+ tumor cells suggesting that s-SHIP/GFP cells were more resistant to drugs. We want now to investigate resistance to other drugs and perform the transcriptomic analysis of these s-SHIP/GFP positive resistant cells to understand the underlying molecular mechanisms.

P6 - Study of the role of MUC1 on the properties and phenomena of chemoresistance to cisplatin in lung cancer cells.

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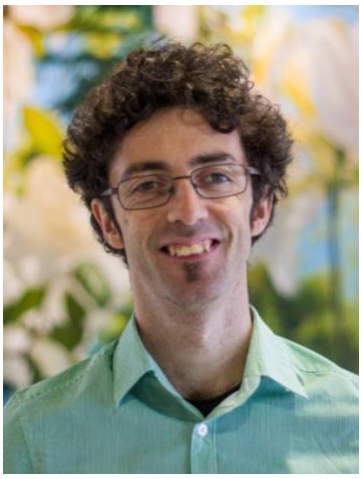
Lung cancer is the leading cause of cancer death worldwide, killing 1.6 million people each year. Non-small cell lung cancer subtype (NSCLC) represents 85% of lung cancers. It is often diagnosed at a locally advanced stage where surgery is impossible, which requires for most cases a treatment based on cytotoxic chemotherapies with platinum salts in combinaison with immunotherapies, which target immune checkpoints, or targeted therapies. Nevertheless, a large number of patients has a primary or secondary resistance to these drugs. MUC1 is a membrane mucin overexpressed in two-third of cancers including NSCLC and is known to play a role in tumor progression, chemoresistance and immunosuppressive microenvironment. In this context, the project aims to better understand MUC1 roles on lung cancer cells properties, chemoresitance to cisplatin and immunosupression.

In this study, we used two lung cancer cells lines invalidated for MUC1 expression (H1975; H1299) and another overexpressing MUC1 (PC9). MTS and proliferation assays, Western blotting and qPCR were used.

Our results show that MUC1 expression (i) is associated with increased cell survival and proliferation, (ii) leads to chemoresistance to cisplatin, (iii) increases the expression of ABC family efflux pumps, (iv) can induce an immunosuppressive microenvironment by increasing PD-L1, IL4, IL13 for PC9 and H1975 and IL10 for H1975 and finally (v) increase the expression of stem cell markers as SOX2 and Nanog.

In conclusion, our results show that MUC1 is an actor in tumour progression and chemoresistance in NSCLCs.

O4 - Modulation of senescence-associated mechanisms in cancer therapy



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***Objective*:** Cellular senescence is a potent tumor suppressive mechanism. However, senescent cells induced by anti-cancer therapy seem to accumulate and persist in tissues generating a pro-tumorigenic environment. The identification of anti-senescence interventions hold the potential to improve cancer treatment.

***Methods*:** Senescent cells are highly heterogeneous. For this reason, various cell-intrinsic and -extrinsic need to be considered. Here, we study the development of senescent cells under various conditions to define phenotypical signatures and predict drug targets.

***Results*:** Our results show that the senescence heterogeneity can be exploited to identify potent senotherapies that have the ability to counteract the detrimental functions of senescent cells during cancer treatment. We discuss compounds that can selectively eliminate senescent cells (senolytics) and compounds that interfere with the secretory profile of senescent cells (senomorphics). In addition, we demonstrate that certain anti-cancer interventions generate a senescent subpopulation with reduced toxicity that can be better tolerated.

***Conclusion*:** Overall, our data provide a solid demonstration that therapy-induced cellular senescence has pro-tumorigenic functions and promotes various adverse reactions. However, we also demonstrate that is possible to target or attenuate detrimental senescence with consequent improvement of efficacy and reduction of toxicity of cancer treatments.

O5 - Deciphering the PD-1/PD-L1 calcium signature in the immunological synapse: microfluidic single cell technology towards precision immunotherapies

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Introduction. Tumor dormancy and cancer cell escape from the immune response represent the major causes of relapse including acute myeloid leukemia (AML), however the mechanisms are still poorly understood. Cytotoxic lysis of tumor cells by CD8+ T cells depends on calcium signaling. However, this cytotoxic activity can be modulated by the tumor cells PD-L1 expression. This project consists in understanding how the PD-1/PD-L1 signaling established during the immunological synapse (IS) between T cells and AML cells modulates calcium signaling

Methods. Using AML patient samples, we assess the PD-1/PD-L1 axis impact on the calcium signaling of CD8+ T cells and leukemia cells according to their phenotype. PD-L1+ leukemic cells will be sorted according to their proliferative status and brought into contact with CD8+ T cells expressing PD-1 in microfluidic devices, enabling optimization of IS formation and molecular studies of cellular events at the single cell scale. Calcium signaling and cellular events are evaluated via calcium imaging and confocal microscopy

Results/expected results. We studied the calcium response of isolated T cells and different conjugates formed according their phenotypes. The conjugates are fixed and permeabilized for immunocytochemistry to confirm IS by observing reorganized actin filaments. A parallel experiment in flow cytometry validates cytotoxic lysis on the same conjugates and supernatants recovery allows to verify by ELISA T cells IFNg and IL-2 secretion

Conclusion. Better knowledge of these regulatory mechanisms leading to immune escape and minimal residual disease may provide new perspectives for immunotherapies or optimization of chemotherapy protocols currently used in the clinic

O6 - In Vitro Study of the Role of TRPM7 Kinase in Metastatic Mechanisms of Pancreatic Cancer Cells

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Metastasis development and chemoresistance are the main causes of poor survival in pancreatic cancer. The TRPM7 protein, a cation channel with the particularity of having an alpha kinase, has been identified to be overexpressed in pancreatic cancer tissues. TRPM7 is involved in many physiological processes and is identified as an important player in the proliferation, migration, and invasion of different cancer cell types. In pancreatic cancer, TRPM7 is described as involved in invasion and migration mechanisms.

However, while the role of the channel in these processes has been studied, the role of the alpha-kinase is still unknown. The objective of this work is to elucidate in vitro the role of TRPM7 kinase in the metastatic mechanisms of pancreatic cancer cells.

PANC-1 human pancreatic cancer cells were modified by CRISPR-Cas9 to obtain an endogenous deletion model of the kinase domain. We characterized this model and observed that the absence of the kinase leads to a decrease of both cell migration and invasion. We also showed that the absence of the kinase leads to an increase of E-cadherin expression associated with a decrease of vimentin expression. These results strongly suggest the involvement of TRPM7 kinase domain in the epithelial-to-mesenchymal transition (EMT).

These first results gave a role of the kinase in the migration and invasion properties of human pancreatic cancer cells. The signaling cascades altered by the absence of this kinase still need to be evaluated. Therefore, this work could designate TRPM7 alpha kinase as a potential therapeutic target.

P7 - Involvement of TrkA/CD44v3 signaling in metastasis formation in triple negative breast cancer

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In 2020, breast cancer was the most common cancer with 2,260,000 people affected and 685,000 deaths worldwide. Among these cancers, triple-negative breast cancer (TNBC) is the most deleterious, with a median survival of 17 months after metastasis diagnosis. In order to understand the mechanisms of metastasis formation in TNBC, the laboratory has identified the overexpression and the involvement of a tyrosine kinase receptor, TrkA. Initial trials with inhibitors of its phosphorylation were not clinically conclusive and the laboratory subsequently demonstrated the involvement of phosphorylation-independent pathways involving the CD44v3 receptor. However, the signaling partners of these independent pathways are still unknown.

To elucidate the mechanisms underlying the involvement of TrkA/CD44v3 signaling in TNBC, different methods are used. First, immunoprecipitations are performed to determine whether the signaling partners are recruited by TrkA or CD44v3. Secondly, to confirm the results obtained by immunoprecipitation, immunofluorescences are performed and analyzed using colocalisation. Thirdly, dynamic modeling is used to define the nature of the interactions between TrkA and the signaling partners. The results show the recruitment of a partner by TrkA independently of CD44v3. Furthermore, this recruitment would be via a direct interaction between TrkA and its signaling partner.

P8 - Role of androgens in SARS-CoV-2 viral infection and COVID-19 progression

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Men with COVID-19 are more likely than women to be hospitalized, admitted to intensive care or die from the disease. Physiological effects of androgens are among the factors that may contribute to this difference. Furthermore, it is already known that the expression of the TMPRSS2 gene, which encodes a crucial protease for virus entry, is regulated by androgens in prostate. Our aim is to investigate the effect of gene expression modulation by androgens, in particular TMPRSS2, on SARS- CoV-2 infection both in vitro in a prostate cell model and in vivo in an animal model and in humans.

We selected a hormone-dependent cell line stably overexpressing ACE2, the protein required for SARS-CoV-2 infection, to measure the effect of hormonal modulation of the TMPRSS2 gene on SARS- CoV-2 infection. The results show that the absence of androgen decreases viral infection, and particularly viral entry, via the loss of TMPRSS2 expression. Conversely, testosterone increases the rate of viral infection.

In vivo, to study the effect of androgens on SARS-CoV-2 infection and disease severity over time, we used a hamster model, for which we performed androgen suppression by castration. Our results show an earlier pulmonary inflammatory response in castrated hamsters compared to non-castrated ones, assessed both by pathological diagnosis and by monitoring inflammatory cytokines. This shift in kinetics in response to SARS-CoV-2 infection reveals an effect of androgens in the lung via an altered transcriptional program.

Our results indicate a role for androgens in the SARS-CoV-2 infection process and in the kinetics of disease progression.

P9 - Nasopharyngeal Carcinoma Exosomes Modulate the Properties of Human Dendritic Cells and Favour their Recruitment

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Introduction: Nasopharyngeal carcinoma (NPC) is dominated by regulatory T cells (Tregs) and NPC tumor exosomes (NPC-Exo) inducing an immunosuppressive microenvironment. Previously, we have showed that NPC-Exo favoured the suppressive activity of Treg and their recruitment by the CCL20 chemokine. The main objective of this study is now to investigate whether NPC-Exo could alter dendritic cell (DCs) maturation and promote tolerogenic DCs (tDCs) commonly known to promote T lymphocyte suppression by inducing Treg. Moreover, we aim to **(i)** define the metabolic status of DCs induced by NPC-Exo (NPC-ExoDC), **(ii)** analyse IDO enzyme expression and activity, and finally **(iii)** highlight the chemoattractive properties of NPC-Exo and the potential involvement of CCL20.

***Methods-Results*:** Phenotypically, we analyzed the expression of maturation markers and the metabolism status, using respectively flow cytometry and Seahorse® technology. NPC-ExoDC exhibit a mature phenotype with a metabolic state similar to control mDCs. Functionally, using proliferation assay, NPC-ExoDC decreased the proliferation of total CD3 T lymphocytes correlated with a decreased production (ELISA assay) of pro-inflammatory cytokines (IL-6, Il- 12p70). Using HPLC dosage of tryptophan metabolites, we observed that after differentiation, NPC-ExoDC exhibit a high Kynurenine/Tryptophan ratio and a western blotting IDO expression compared to DC controls. Finally, chemoattractive properties of NPC-Exo on DCs were tested by video-microscopy chemoattractive assays suggesting that NPC-Exo could preferentially attract NPC-ExoDC comparatively to control mDC, but not in a CCL20-dependant manner.

***Conclusion*:** Our results describe the major role of NPC-Exo in promoting immune tolerance within the NPC microenvironment and so identify potential new anti-tumoral therapeutic targets.

P10 - Identification of a chemosensitizing miRNA by a functional screening and characterization of associated target genes: towards new therapeutic strategies for ovarian cancers

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Introduction. The clinical management of ovarian cancer constitute a real challenge that requires novel therapeutic strategies. miRNAs hold promise by playing a critical role in determining the cell phenotype. In fact, the several hundreds of targets they regulate could constitute vulnerabilities for cancer cells.

Methods. A functional miRNAs screening and real-time continuous cell monitoring was performed in two chemoresistant ovarian cancer cell lines in order to identify cytotoxic miRNAs in association with chemotherapy (cisplatin). Transcriptomic and bioinformatic studies were done to characterize the molecular determinants involved in the cytotoxic action of miRNA candidates.

Results. We identified 16 miRNAs that sensitize the two chemoresistant ovarian cancer cell lines and we focused on a miRNA candidate which had a strong activity and had not been studied yet. Individual functional studies have confirmed its cytotoxic action when combined with cisplatin on three chemoresistant ovarian cancer cell lines (IGROV1-R10, OAW42-R and SKOV3). Transcriptomic data were then overlapped with predicted targets. Among them, several are genes involved in DNA repair mechanisms, and more specifically involving homologous recombination. These genes are currently being analyzed.

Conclusion. The identification of targets and pathways regulated by miRNAs that sensitize cell lines to cisplatin could lead to a better understanding of resistance mechanisms in ovarian carcinoma. It could also lead to the discovery of new therapeutic strategies in association with platinum derivatives.

P11 - ABSP : A new automated R tool to analyze Bisulfite Sequencing PCR (BSP), to facilitate the study of target regions DNA methylation.

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Introduction. DNA methylation is one of the most studied epigenetic process in mammals. By regulating gene expression, it participates in cancer development and resistance to therapies. Both hypermethylation of tumor suppressor genes and hypomethylation of oncogenes can serve as biomarkers for diagnosis and prognosis of patients undergoing therapies. And, as it is a reversible mechanism, the targeting of DNA methylation can be an interesting therapeutic approach. Therefore, it raises the necessity to study it efficiently with the appropriate methods and tools.

Methods. Among the methods used to estimate DNA methylation, the Bisulfite Sequencing PCR (BSP) is one of the most accessible and affordable. It relies on the bisulfite conversion of unmethylated cytosines into uracils while methylated cytosines remain unchanged. After PCR amplification in which uracils are replaced by thymines, the sequencing of products directly (direct-BSP) or of cloned products (cloning-BSP) allows the evaluation of DNA methylation percentages among the DNA molecule population.

Results. The analysis of BSP results is tedious and time-consuming, that is why several tools have been developed to facilitate it. The 'Analysis of Bisulfite Sequencing PCR' (ABSP) tool offers many advantages compared to the existing tools: (1) it can analyze both types of BSP (analysis strategies of direct-BSP and cloning-BSP differ), (2) the R programming language provides great accessibility, adaptability, flexibility and is new for this use, (3) its analysis process is complete, from the methylation percentage calculation to data visualization and comparative statistics, and (4) its use is completely automated for the user, from data input to publication-ready graph generation.

Conclusion. The ABSP tool facilitates the study of DNA methylation at target regions for researchers and proposes a novel approach of fully automated, yet flexible, analysis of data using the R language.

P12 - Sodium – Calcium Signaling Undergoing Metastatic Potential of Prostate Cancer cells

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Despite considerable progress in terms of diagnosis and treatment, prostate cancer represents the third most cause of death with more than 375,000 deaths per year. The treatment options are limited after the tumor has metastasized. A new model has been generated from circulating tumor cells (CTC) which will help us to have deeper insights in understanding the mechanisms involved. Genomic instability is a critical feature of human cancer. Among the genes affected, those encoding ion channels are present. Previous study from our laboratory have described that ion channels control some of the "hallmarks of cancer" such as tumor angiogenesis, migration, and metastasis, thereby paving the way to a new chapter in oncology. Recently we have performed bioinformatic analysis of prostate tumors, revealing several mutations of NALCN, a sodium channel which we previously described as actor of invasion (a crucial step before metastasis) during prostate cancer (PCa). During my thesis, I am investigating ; 1) the ion homeostasis of circulating tumor cells (CTC) and 2) The role(s) of newly reported NALCN mutations during prostate cancer progression.

P13 - IRE1 RNase controls CD95-mediated cell death.

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Unfolded Protein Response (UPR) and Death Receptor (DR) signalling are cellular stress pathways frequently activated towards pro-tumoral cellular outputs in cancer. Experimental evidence has highlighted functional links between the UPR and signalling by the DR TRAIL-R1/2. Herein, we demonstrate that the UPR sensor IRE1 controls the expression of the DR CD95/Fas, and its cell death-inducing capacity. Whereas CD95 is not a general determinant of ER stress-induced cell death, IRE1 RNase activity inhibition increased CD95 expression and exacerbated CD95L-induced cell death in glioblastoma (GB) and Triple-Negative Breast Cancer (TNBC) cell lines. In accordance, CD95 mRNA was identified as a target of the Regulated IRE1-Dependent Decay of RNA (RIDD). Moreover, CD95 expression is elevated in TNBC and GB human tumours exhibiting low RIDD activity. Surprisingly, CD95 expression is also reduced in XBP1s-low human tumour samples. We show that IRE1 RNase inhibition led to CD95 expression attenuation and reduced CD95-mediated hepatic toxicity in mice. In addition, overexpression of XBP1s sensitized GB and TNBC cells to CD95L- induced cell death. Overall, these results demonstrate the tight IRE1-mediated control of CD95-dependent cell death signals in a dual manner through both RIDD and XBP1s, and they identify a pharmacologically actionable link between IRE1 and CD95 signalling.

P14 – SENSARCOME : Targeting radio-induced senescence to prevent secondary sarcomas in irradiated field

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One rare secondary effect of radiotherapy is the development of second cancers, including sarcomas which have a bad prognosis. These secondary sarcomas preferentially developed not inside the targeted volume but around, after a latency period of 5 to 30 years.Previous studies of the laboratory show that ionizing particles diffusing from the treated volume to the margin are responsible for an accumulation of DNA single-strand breaks (SSBs) in the margin cells, resulting in a senescent phenotype. A few of these senescent cells are able to re-enter in the cell cycle to generate a filiation of mutated cells that could be at the origin of the second sarcomas (Goy et al, eLife, 2022).

Since the absence of SSB repair is crucial for the induction of senescence, we wanted to characterize the cause of the repair default. We have shown that the non-repair of SSBs is associated with a decrease in PAR (poly ADP-ribose) foci formation. To explain this decline, we examined the expression of the enzymes involved in PAR synthesis and degradation. The first RT-PCR and western- blots results show (i) a decrease in the expression of PARP1 and PARP2, the main enzymes involved in PAR synthesis, (ii) an increase in the expression of HPF1, a partner of PARP1 known to favor the synthesis of shorter PAR chains, and (iii) a increase in PARG expression, the main enzyme involved in the degradation of PARs, at the mRNA level, to be confirmed at the protein level.

P15 - Identification of Merkel cell polyomavirus' oncogenic interactions

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The Merkel Cell Carcinoma, a rare and yet very aggressive skin cancer caused in 80% of the cases by the Merkel Cell PolyomaVirus. The VP-MCCs harbor a low somatic mutational background combined to the expression of only two viral proteins sufficient and necessary for cancer initiation and maintenance making the VP-MCCs a simple disease model for in depth studies of transforming mechanisms.

My PhD project aims to understandthe transforming capabilities of these viral proteins on a given cell. In order to achieve that, we combine an interactomic study using a proximity-dependent biotin labelling: BioID and proteomic studies following the ectopic expression of the T antigens.

We identified 481 interactors, including most of the reported partners. We used the protein expression to determine the transcription and epigenetic factors that were likely responsible for the observed expression pattern. The comparative analysis of the interactomic and the proteomic data led to the identification of several epigenetic factors and complexes that seem to bear an important role, including the few ones that are known to be involved in MCCs oncogenesis. These factors are under further study to assess the importance of their role in MCCs.

The possible cooperation between the T antigens is also being tested using a new innovative complementation-based proximal interactomic tool: Split-TurboID. Preliminary results suggest a direct collaboration between the two T antigens. Together, our works open novel avenues to better understand MCC oncogenesis and basal cellular mechanisms that seem disrupted in those neoplasias.

P16 - TRPM4 regulates cytosolic Ca2+ oscillations and secretome in chemotherapy-induced senescence

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Cellular senescence is characterized by a stable cell cycle arrest, various macromolecular changes, and a hypersecretory, pro-inflammatory phenotype- the senescence-associated secretory phenotype (SASP). During chemotherapeutic treatment, DNA damaging agents may induce senescence in benign cells of the tumor microenvironment resulting in SASP production that act in a paracrine manner promoting tumor resistance phenotypes. Here, by q-RT-PCR, we show that TRPM4 is upregulated in response to DNA-damaging chemotherapeutic drugs in prostate stromal cells. By western blot analysis, we identify that the isoform that is upregulated represents the channel's dominant negative, short isoform, rather than the wild type, full-length isoform. TRPM4 appears to reshape Ca^{2+} homeostasis and control the oscillatory behavior of persistent DNA damage-induced- senescent cells. Moreover, we show that conditioned medium from senescent stromal cells enhances the invasive capacity of epithelial prostate cancer cells, which can be limited by silencing TRPM4 in stromal cells.

Our results suggest TRPM4 as a novel tumor microenvironment regulator in prostate cancer progression in response to chemotherapy.

P17 - The role of TNF-alpha in thymus dysfunction during AML

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Acute myeloid leukemia (AML) is characterized by an increased proliferation of hematopoietic progenitors or precursors (blasts) of the different myeloid lineages. Studies performed in AML- affected patients revealed a T-cell immunodeficiency, characterized by a decreased number of peripheral T lymphocytes' TRECs and a restricted repertoire. To study thymus dysfunction during AML, we used an AML mouse model in which we previously showed a thymic atrophy notably due to an increased cell death among double positive (CD4+CD8+) thymocytes.

To better understand this massive thymocytes' loss, we collected *ex vivo* thymi from control and leukemic mice and immunophenotyped them for cell death. In parallel, we also assessed for the expression of different actors of cell death signaling pathways by RT-qPCR or Western Blotting. When comparing leukemic to control mice, there was a significant increase in the expression of *Mlkl* gene, phosphorylated MLKL and RIPK3 proteins and TNF-alpha receptors on double positive (CD4+CD8+) thymocytes. These findings revealed an abnormal cell death of double positive (CD4+CD8+) thymocytes by necroptosis (in addition to apoptosis) during AML. Such cell death was also observed *in vitro* using cultured wild-type thymocytes and recombinant TNF-alpha protein in the presence or absence of apoptosis inhibitors. Thus, we demonstrated that TNF-alpha plays a deleterious role in thymic function during AML by contributing to extensive thymocytes' loss. Further investigations will help to better characterize its impact on the peripheral T-cell repertoire and antigens recognition.

P19 - The first peptide ligand targeting the EGF2 domain of MUC4 rescues Herceptin accessibility in pancreatic cancer cell in vitro

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Pancreatic cancer remains one of the most lethal malignancies. This cancer survival rate has remained unchanged since the 1970's, whereas its incidence is constantly increasing. Moreover, this cancer exhibits no efficient treatments, since conventional therapies often remain inefficient or fail. So, these problems raise this cancer as a serious problem of public health, for which new therapeutic targets are urgently needed. In this way, the MUC4 oncomucin is highly regarded as a potent target as it is neo-expressed in early neoplastic stages and involves in ErbB2 targeted therapies (Herceptin) resistance. Also, our recent work has shown that from the EGF domains of MUC4 depend the interaction and the oncogenicity of the MUC4-ErbB2 complex. Therefore, they could be targeted to modulate ErbB2 oncogenic pathway and decrease cancer cells proliferation. To this aim, we have designed the first peptide ligand targeting the MUC4EGF2 domain and characterized its anti- proliferative effects in pancreatic cancer cells.

In this work, by developping several strategies of protein-protein interaction (GST pull-down, co-immunoprecipitation, MicroScale Thermophoresis), we first show that the peptide ligand specifically binds the EGF domains of MUC4. Then, we prove that the peptide acts as an inhibitor to disrupt the MUC4-ErbB2 complex and decrease pancreatic cancer cell proliferation, by impairing MUC4EGF-mediated ErbB2 signaling activation. Finally, we show that the peptide rescues the Herceptin accessibility to ErbB2 in vitro.

Together, these results demonstrate that the targeting of MUC4EGF domains represents a new alternative strategy to overcome ErbB2 therapeutic failures in pancreatic cancer.

P20 - Istradefylline (KW6002) protects from cisplatin-induced nephrotoxicity while preserving cisplatin anti-tumor effects

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Cisplatin is a potent chemotherapeutic drug, widely used in the treatment of various solid cancers. However, its clinical effectiveness is strongly limited by frequent severe adverse effects, in particular nephrotoxicity. Renal toxicity of cisplatin is cumulative and dose- dependent, leading to tubular lesions associated with a lower glomerular filtration rate. Cisplatin has also been reported to induce acute renal failure in up to 35 % of patients, leading to cisplatin dose adjustment or even withdrawal, thereby adversely affecting patients' outcome. Therefore, there is an urgent medical need to identify novel strategies limiting cisplatin-induced toxicity.

In this context, we provide evidence that the renal expression of the adenosinergic A2A receptor, which is involved in tissue/cellular homeostasis, is induced in several mouse models of cisplatin intoxication. Moreover, the FDA-approved adenosine A2A receptor antagonist istradefylline (KW6002) significantly protects from cisplatin-induced nephrotoxicity in mice without or with tumors. Moreover, we also demonstrate that the anti-tumoral properties of cisplatin are not altered by istradefylline in tumor-bearing mice and could even be potentiated. Altogether, the present results support the use of istradefylline as a new valuable preventive approach for the clinical management of patients undergoing cisplatin treatment.

P21 - Mechanobiological characterization of a 3D in vitro pancreatic ductal adenocarcinoma model and the study of tumor-stroma interaction

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Pancreatic ductal adenocarcinoma (PDAC) is 4th leading cause of cancer mortality and is projected to become 2nd by 2030. It has a very bad prognosis as it is mostly diagnosed during its late stages. In order to better reproduce PDAC, its main characteristics have to be restituted. This includes a dense stroma composed of a large population of fibroblasts overexpressing extracellular matrix (ECM) proteins. This elevated density increases the stiffness and decreases mass transport within the tumor, in turn increasing drug resistance. Our aim is to create a model in which we will reproduce physical characteristics: interstitial flow, varying levels of stiffness with the integration of a pertinent ECM and apply different levels of compression.

Our models are either made of patient-derived PDAC tumoroids or co-culture of human pancreatic cancer cell lines with activated human pancreatic stellate cells. The culture microenvironment is an ECM composed of hyaluronic acid and collagen I with an adjustable stiffness (1;8;16 kPa). The stiffness impact on protein expression is studied by Western blotting and immunofluorescence staining of tissue sections.

Our results show that the set-up of the matrix in a co-culture system recapitulates the expression of specific epithelial (E-cadherin) and mesenchymal (vimentin, α-SMA) markers, tumorigenic signaling pathways (β-catenin, MAPK) and mechanobiological actors (YAP/TAZ pathway). Having shown that the ECM fits with our model, we plan now to develop a pancreatic tumor- on-chip within a microfluidic device that increases the control over crucial parameters such as compression and stiffness, to study PDAC physical properties and drug resistance.

07 - Altered glycosylation in cancer: dissecting the molecular mechanisms and understanding the clinical implications

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Objective: Alterations of glycosylation are common molecular alterations with major biological implications for cancer progression. Cancer is a heterogeneous disease that requires multidisciplinary treatment. Current targeted therapy depends on patient stratification based on molecular features of the tumor.

Methods: This presentation will report on the basis of alterations of glycosylation that occur in cancer. Recent results applying glycomic and glycoproteomic strategies in human cancer that provided novel information with major clinical implications.

Results: Our results show that the alterations of glycosylation impact the activation of oncogenic receptors in tumour samples, such as RON, MET, EGFR and HER2 (ErbB2). I will also report on the glycoproteomic map of the HER2 in gastric cancer cells which disclosed a site-specific glycosylation profile of this receptor in gastric cancer cells and how this HER2 glycosylation affects the biology of the receptor and the sensitivity of HER2-dependent gastric cancer cells to the therapeutic humanized monoclonal antibody trastuzumab.

Conclusion: Overall, our results highlight the functional aspects of glycosylation modifications occurring in cancer and supports their potential application as biomarkers for patient stratification, personalize medicine and for novel and improved therapeutic applications.

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08 - In search of the best antibody format for immune checkpoint inhibitors

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Antibodies targeting immune checkpoints must be considered in reality as a heterogenous family of immunostimulatory antibodies displaying very different mechanisms of action, not only depending on the target or on the cells expressing it, but also on the IgG subclass or IgG variant that has been chosen. To dissect this complex landscape, the clinical experience has been confronted with a precise analysis of the heavy chain isotypes, according to a new Ge (G engineering) nomenclature.

For antibodies targeting inhibitory receptors, anti-CTLA-4 antibodies (whose main effect is to kill regulatory T cells) have to be distinguished from anti-PD-1 antibodies and other true antagonistic antibodies. Antibodies targeting ligands of inhibitory receptors (PD-L1, CD47) represent another different category, due to the antigen expression on tumors and a possible beneficial killing effect. The case of agonistic antibodies targeting lymphocyte activatory receptors, such as CD40 or 4-1BB, is still another "under construction" category because these products are less advanced in their clinical development.

Altogether, it appears that choosing the right heavy chain is crucial to obtain the desired pharmacological effect in patients.

O9 - Role of Galectin-9 in the Induction of Tolerogenic Dendritic Cells Mediated by Nasopharyngeal Carcinoma Exosomes

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Introduction: Nasopharyngeal Carcinoma (NPC) microenvironment is dominated by regulatory T lymphocytes and tumor-derived exosomes (Exo-NPC) both presenting immunosuppressive properties. Preliminary results of the laboratory have shown that Exo-NPC carrying Galectin-9 (Exo- NPC-Gal9+) induce dendritic cells with tolerogenic properties. In this context, our objective is to investigate more precisely the role of Galectin 9 (Gal-9) in these induction mechanisms in order to propose an immunotherapy targeting Exo-NPC.

Results: We generated dendritic cells (DC) from human monocytes in presence of recombinant Gal- 9S (DC-Gal9) or Exo-NPC-Gal9+ (DC-Exo-NPC-Gal9+). The state of maturation of the DCs was then validated at the phenotypic and functional level. DC-Gal9 and DC-Exo-NPC-Gal9+ express maturation markers similarly to maturation control (mDC). Unlike DC-Exo-NPC-Gal9+ which secretes few pro- inflammatory cytokines, DC-Gal9 has also a cytokine secretion profile identical to mDC. Nevertheless, our results suggest that both DC-Gal9 and DC-Exo-NPC-Gal9+ have immunosuppressive properties by inducing a decrease of the proliferation of CD3+ T lymphocyte. Interestingly, blocking Gal-9 by an anti-Gal-9 monoclonal antibody (patented by the laboratory) seems to inhibit the suppressive function of DC-Gal9 by restoring LTCD3+ proliferation. Moreover, blocking exosomal Gal-9 using this monoclonal antibody seems also to inhibit partially the suppressive function of Exo-NPC-Gal9+ by restoring the proliferation of autologous PBMCs.

Conclusion: These results show for the first time that recombinant Gal-9 and Exo-NPC-Gal9+ do not impact DC maturation but seem to play a role in the induction of DC with tolerogenic properties. Interestingly, the use of an antibody targeting Gal-9 seems to reverse this immunosuppression, leading to promising therapeutic prospects.

O10 - IL-2 is inactivated by the acidic pH environment of tumors enabling engineering of a pH-selective mutein

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Cytokines interact with their receptors in the extracellular space to control immune responses. How the physicochemical properties of the extracellular space influence cytokine signalling is incompletely elucidated. Here, we show that the activity of interleukin (IL)-2, a critical cytokine in T cell immunity, is profoundly affected by low pH (~6.5), limiting IL-2 signalling in a IL-2Rα-dependent manner. Generation of lactic acid by tumours limits STAT5 activation, effector differentiation and anti-tumour immunity by CD8+ T cells and renders high-dose IL-2 therapy poorly effective. Directed evolution by yeast display enabled selection of a pH-selective IL-2 mutein (Switch-2). Switch-2 binds the IL-2 receptor subunit IL-2Rα with higher affinity, triggers more potent STAT5 activation and drives CD8+ T cell effector function at acidic pH than at pH 7.2 typical of normal tissues. Consequently, Switch-2 is mainly uptake by CD8+ T cells localized in acidic tissues such as tumour and lymph-node, at the contrary of IL-2 that was found at a greater extent in CD8+ T cells in blood and lungs. High-dose Switch-2 therapy induces anti-tumour immunity in different tumour models (B16, MC38, and 4T1) with reduced on-target toxicity in normal tissues, whereas high-dose IL-2 therapy resulted in toxicity alone. Phenotypical and single- cell analysis on CD8+ tumour infiltrating lymphocytes (TILs) shows that Switch-2 increases cell proliferation, expansion of antigen specific cells, and cytokine expression as compared to IL-2. Therapeutic manipulation of the pH-selective activity of cytokines is a powerful approach to exploit the therapeutic efficacy of cytokines in pathological environments with reduced systemic side effects.

P22 - Deciphering and targeting GD2 ganglioside O-acetylation pathways in neuroectoderm-derived cancers

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The *O*-acetylated form of GD2, almost exclusively expressed in cancerous tissues, is considered to be a promising therapeutic target for neuroectoderm-derived tumors. Our recent data have shown that 9-*O*-acetylated GD2 (9-*O*AcGD2) is the major *O*- acetylated ganglioside species in breast cancer cells but the mechanism underlying GD2 *O*-acetylation remained unclear. In 2015, Baumann *et al.* proposed that Cas 1 domain containing 1 (CASD1), which is the only known human sialyl-*O*- acetyltransferase, plays a role in GD3 *O*-acetylation1 but the mechanism of GD2 *O*-acetylation remains poorly understood. We analyzed the possible role of CASD1 in GD2 *O*-acetylation in breast cancer (BC) cells, using triple negative SUM159PT cells that endogenously express *O*AcGD2 as a model. The modulation of CASD1 expression using transient transfection strategies in triple negative breast cancer cells provided interesting insights into the role of CASD1 in *O*AcGD2 and *O*AcGD3 biosynthesis, and it highlights the importance of further studies on *O*-acetylation mechanisms2. Consequently, in order to identify additional genes involved in OAcGD2 biosynthesis in BC, we performed a kinome/phosphatome siRNA screen and identified genes that up- or down-regulate OAcGD2 expression. *CERK* (ceramide kinase gene) was selected for further studies among genes of interest. Ceramide kinase, the enzyme that synthesizes ceramide-1-phosphate from ceramide, has a direct link with glycosphingolipid biosynthesis that starts with the conversion of ceramide into glucosylceramide. In addition, *CERK* inhibition by siRNA induced a significant increase of OAcGD2 expression in BC cells in the RNAi screen. We confirmed the effect of *CERK* inhibition on OAcGD2 expression using pharmacological inhibitors and individual siRNA in different BC cell lines, and studied the impact of *CERK* inhibition on the malignant properties of BC cells. Our data highlight the potential of increasing the efficacy of OAcGD2-targeted immunotherapy with compounds such as *CERK* inhibitors that increase OAcGD2 expression.

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P23 - MET receptor and ETS fusions : Co-actors in the metastatic progression of prostate cancer

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Introduction: Prostate cancer (PCa) has the highest incidence among male cancers in European and American countries. In advanced stages, which may be metastatic, there is a high mortality rate. MET receptor and ETS transcription factors (ERG and ETV1) are important actors in PCa progression. MET is overexpressed in hormone-resistant tumors and in bone metastasis. ETS can be overexpressed all along the disease. Interestingly, there are many functional links between MET receptor and ETS transcription factors suggesting their belonging to the same regulatory pathway. The aim of our study is to understand the collaboration between these two actors in PCa.

Methods: Cellular models expressing ERG/ETV1 and MET, *in vitro* phenotypic tests, *in vivo* tests in humanized mice

Results: In vitro phenotypic tests showed that, ERG and ETV1 transcription factor induce more migration/invasion capacities and activation of MET signalling amplified these responses. In vivo subcutaneous injection in humanised HGF mice showed that of ERG/ETV1 overexpressing cells leads to bigger tumors. Moreover, administration of a Tyrosine Kinase Inhibitor (capmatinib) blocking MET signalisation, considerably reduced the tumoral volume induced by the expression of ERG and ETV1.

Discussion: Our results show for the first time, a collaboration between MET receptor and ERG/ETV1 transcription factor leading to more aggressive phenoype and tumors in our PCa models.

P24 - Targeted PDT for intraperitoneal ovarian cancer, a novel way to stimulate anti-tumoral immune response

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***Introduction*:** Ovarian cancer (OC) is one of the most defying diseases in gynaecologic oncology. Even though surgery remains crucial in the therapy of patients with primary OC, recurrent recidivism calls for the development of new therapy protocols for patients dealing with this cancer. Photodynamic Therapy (PDT), which use a combination of oxygen, a photosensitizer (PS) and a specific light have shown improvements in cancer treatment and in the induction of an anti-tumoral immune response. In order to target specifically peritoneal metastasis, which overexpress FRα in 80% of cases, a new-patented PS coupled with folic acid has been developed in our team. Herein we propose PDT using this new patented PS applied in an in vivo mice model.

Methods and Results: The efficacy of the treatment was evaluated in mice without and with PBMC reconstitution. When mice were reconstituted and upon PDT, the fold of tumor decrease was higher than not reconstituted mice. An immune response was activated decoded with an increase in NK, CD3+, LT helper and Cytotoxic T cells. Thereafter, an increase in the secretion of the cytokines IFNγ and TNFα were noticed while an inhibition in TGFβ, IL8 and IL10 accompanied this immune response activation.

Conclusion: Therefore, our work has shown for the first time that a fractionized PDT protocol using a folate-targeted PDT is effective for treatment of OC. The interest in using PDT in this case, goes beyond the local induction of tumor cell death, but can promote subsequent anti-tumor response.

P25 - Development of therapeutic targeting in lung cancer with MET ex14 mutation and co-alterations.

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Lung cancer is the leading cause of cancer-related deaths worldwide. The discovery of molecular alterations responsible for oncogenesis has paved the way for precision cancer medicine using targeted therapies as tyrosine kinase inhibitors (TKIs) and specific antibodies. Mutations in the splice sites of exon 14 of the MET receptor kinase (MET ex14) are detected in 3% of lung cancers and lead to the loss of a regulatory domain. Although half of MET ex14 patients respond to MET inhibitors (MET TKI), these results are lower than those obtained with other receptor tyrosine kinase inhibitors. MET ex14 mutations are frequently associated with other alterations including PTEN, KRAS, PIK3CA or autosecretion of HGF, the ligand of MET. We aim to determine whether these co-alterations may be factors of sensitivity or resistance to TKIs and thus better predict the benefit of these therapies to patients. Our second objective is to identify which therapies could overcome these resistances. While autocrine secretion of HGF does not induce a significant effect on tumor growth in vivo, loss of PTEN expression leads to strong growth that cannot be suppressed by the use of a TKI-MET alone. Currently, we are developing a relevant 3D BIOMIMESYS® matrix spheroid assay model to assess the response to MET inhibitors in order to further characterize the impact of MET ex14 co-alterations. This will allow the identification of effective treatment combinations or new molecules that will then be tested in vivo in human SCID-HGF transgenic mice.

P26 - Characterization of original MET mutations in hereditary papillary renal cancer

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Introduction: In several cancers, the receptor tyrosine kinase MET is activated by mutations leading to its constitutive activation. Importantly, targeted therapies directed against MET kinase (MET TKI) have been approved very recently to treat these patients. However, democratization of high through put sequencing leads to continuous discovery of novel MET mutations. Thus, the current challenge is to establish whether these variants are activating mutations involved in tumor progression and whether MET TKI could be effective on them.

Methods: Through a collaboration with the Institute Gustave Roussy, which centralized hereditary papillary renal carcinoma (HPRC) characterized by the presence of MET mutation in more than 80% of them, we identified 8 original MET mutations. All these mutations were reconstituted in cell lines and MET activation, biological responses and sensitivity to MET TKI were characterized.

Results/conclusion: Our results demonstrate that four MET variants, all located in the P-loop of the kinase domain, lead to MET activation. All of them are sensitive to MET TKI. In addition, we found that HGF stimulation is still able to promote their activity, suggesting importance of ligand expression to potentiate effect of these mutations. In order to confirm the involvement of HGF, reconstituted cell lines with MET mutations will be xenografted in original mouse model humanized for HGF. In parallel, expression of HGF will be assessed in tumor samples of patients displaying such mutations. Our results already suggest that patients harboring these novel MET variants could benefit for treatment with MET TKI.

O11 - Machine learning and multi-omics approaches for the description and modeling of the tumour microenvironment

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Given the recent discoveries about the importance of specific interactions between immune and cancer cells, understanding the spatial properties of tumors at single-cell resolution becomes crucial. We have recently developed computational tools to describe spatial patterns and clustering of specific cell types in tissues using network theory. These approaches allow us to extract statistical properties from imaging or spatial-omics datasets that can be used as biomarkers. We will describe software to extract cellular networks from imaging or spatial-omics datasets (tysserand, Coullomb and Pancaldi 2021) and analyze spatial patterns by defining cellular neighborhood states across lung cancer samples. Some of the identified patterns can constitute biomarkers and aid in prediction of response to immunotherapy.

Finally, we will discuss our planned strategy to achieve an understanding of the dynamics of cellular interactions and phenotype transitions that can help us better target therapies in a personalized medicine approach. These models involve a combination of agent-based and logic modeling to represent processes at play in the tumor microenvironment at different levels. A major challenge remains in bridging the gap between literature based model construction and purely data-driven approaches, which are necessary to make the models patient-specific and clinically relevant.

O12 - Classification of single cancer cells based on their biophysical signatures

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Cancer cells present a wide range of properties due to their heterogeneity. Analysing this heterogeneity demands distinguishing cells at the single-cell level. Thus, we need a practical, label-free and rapid method to characterize a massive number of cells. Among different properties, biophysical ones are excellent candidates for practical purposes as they do not require any pre-treatments, *e.g.* staining. However, cell biophysical responses can be similar to each other that reliable classification requires in-depth analysis of the results which can only be provided by artificial intelligence. Therefore, we propose applying statistical learning to biophysical properties for cancer cell classification.

We integrated MEMS tweezers with a microfluidic device to measure the biophysical properties of a single cell, *e.g.*, size, stiffness, and viscosity. We tested two breast cancer cell lines with different metastatic potential (MCF7: low and SUM159-PT: high). Our results showed a significant difference between the mean stiffness and viscosity of those two populations. However, the data ranges were overlapping for the majority of the cells (>90%), prohibiting the use of those parameters to distinguish cells individually. Therefore, a generalized additive model analysis was applied to the splines basis projection of the stiffness and viscosity curves. 85 cells were randomly chosen for a training session, and the remaining 20 cells were tested blindly. The training sample was validated by the test data with a correct classification rate of 85%.

To conclude, multi-parameter analysis of single cells leads to the practical identification of individual cells by integrating MEMS measurements with statistical learning algorithms.

O13 - High-throughput biophysical analysis of single cells

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Characterizing circulating tumor cells (CTCs) has been targeted for cancer diagnostics. However, their heterogeneity and low concentration demand single-cell analysis in a high- throughput way. Currently-approved method, which uses surface epithelial biomarkers, suffers from a loss of reliability for cells experiencing changes in their surface properties. Therefore, there is a need for a reliable and high-throughput CTC-detection method which is practical enough for routine medical examinations.

A hybrid microfluidic MEMS device was fabricated to perform impedance cytometry with 3D silicon electrode pairs and mechanical characterization by compressing cells between a sidewall converging into the channel and the tip of a mechanical sensor. Working in a continuous flow format permitted high-throughput measurements whereas sensitive measurements were sustained by keeping all functional MEMS elements in air and accessing the channel via stable air-liquid interfaces. Multi-parameter analyses were realized performing simultaneous electrical and mechanical measurements. The response of each cell was monitored, first, electrically at three different frequencies and, then, mechanically during a compression cycle while flowing continuously. Specifically-designed electrodes provided sensitive electrical measurements, which resulted in characterizing cell properties, such as size, membrane conductivity and cytoplasm resistivity. Similarly, the integrated displacement sensor measured cell stiffness during the compression cycle providing information on cell mechanical properties. The proposed method aims at providing high-throughput biophysical cytometry for cancer cell evaluation in an optics- and marker-free way.

P27 - Lung-RegMap portal : a co-regulatory influence network view of lung cancer heterogeneity.

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Lung cancer studies performed in a variety of laboratories and by a number of large-scale projects have given an unparalleled amount of information on tumors and *in vitro* models. Consolidating these data into an easily accessible and intuitive system-level format is crucial to accelerate systems oncology model development.

We combined network biology with machine learning and visualization tools to execute a cycle of systems oncology model development: inference of the co-regulatory networks (from transformed cells in vitro), interrogation of the tumors in vivo using the inferred networks, and intervention with the network (feeding back to the in vitro tumor models).

First, analysis of the *in vitro* gene expression profiles of 277 lung cancer cell lines of the CCLE with CoRegNet yields to the reconstruction of a co- regulatory influence network (Lung-CoRegNet) that contains 502 TFs/co- TFs linked by 18053 significant co-operativity interactions and regulating 4143 targets genes. Second, a regulatory influence signal Lung-RegMap is built from 28 publicly available datasets representing >4000 patients.

Lung-RegMap allow user to: (1) explore the similarities and differences between cancer subtypes and identify their possible core regulators; (2) identify rare subtypes and inter-heterogeneity (3) define new targets related to the different states and plasticity of the tumours (e.g. therapy sensitive vs resistant cells).

P28 - A Large-Scale Hybrid Model to Study Metabolic Reprogramming in Cancer-Associated Fibroblasts

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The importance of the tumor microenvironment (TME) in cancer's onset and progression is widely recognized nowadays. Cancer-Associated Fibroblasts (CAFs), unique components of the TME, have been identified as active players in disease initiation and crucial contributors to tumor growth, survival, and invasion. The activation of CAFs is associated with metabolic alterations resulting from dysregulation of signaling and gene regulation machineries. Deciphering the intricate mechanisms underlying CAFs' metabolic reprogramming may provide significant insight into their involvement in cancer and provide new therapeutic approaches. Computational modeling, and more specifically hybrid models, represent a real asset in their ability to span multiple biological layers of interest. This work presents the first hybrid CAF model covering signaling, gene regulation, and metabolism. The model combines a cell-specific Boolean regulatory network with a constraint-based human central metabolic network. The automated framework for hybrid modeling exploits the Boolean network's trap- spaces as additional constraints on the metabolic network's reactions. Subsequent flux balance analysis allows the assessment of CAFs' regulatory outcomes' control over their central metabolic flux distribution. The hybrid CAF model is able to reproduce the experimentally observed glycolytic switch in CAFs and the associated reverse Warburg effect. Accordingly, CAFs undergo metabolic reprogramming to turn into "metabolic factories" able to produce high levels of energy-rich fuels and nutrients for neighboring demanding cells. Additionally, a series of *in silico* simulations involving knock-out and knock-in combinations of the regulatory inputs was conducted to identify key players of these metabolic alterations.

O14 - Rest energetic assessment and sensitivity to immune checkpoint inhibitors in oncology

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O15 - Adaptation of breast cancer cells : variability of single cells responses

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One of a key cellular defensive mechanism relies on the link between metabolic flux and oxidative stress exploiting the dualistic role of hydrogen peroxide, acting both as signalling and damaging molecule. Our study presents an experimental approach where the interplay between metabolic flux and oxidative stress is studied in short time-scales, during one hour perturbation of redox homeostasis. In a first step, we are interested on controlling the H_2O_2 stimulus that will be used as a tool to modulate intracellular redox homeostasis. An experimental system is designed, to constantly control the dose applied to breast cancer cell line (MCF7). Using a custom fluidic system, the intracellular H_2O_2 production rate is increasing, by varying the external H_2O_2 concentration. Stimulus delivery and removal is thus performed fast enough (faster than cellular consumption) to study the dynamical cellular responses. In a second step, external H_2O_2 stimulation is applied on living cells, therefore disturbing their internal redox balance. For this purpose, experiments have been designed and performed using fluidic system, following the molecular dynamics at the single cell level, with high- throughput. The cellular response to stress is quantified by targeting key molecules regulating the redox homeostasis. Given that, the dynamics of NADPH and glutathione potential are visualized using time-lapse fluorescence microscopy in cellular cytoplasm of living cells. We notice that pH is a key parameter, changing during metabolic modulation and observed while using two different H_2O_2 sensitive probes, HyPer and Grx1-roGFP2. Monitoring single cells is observed the cell-to-cell variability of response upon H_2O_2 stimulation. Using H_2O_2 as a tool to modulate intracellular redox homeostasis, two short time adaptation mechanisms are noticed: glutathione system is restored in the first 30 minutes during stimulation, while NADPH pool is faster reaching back to the basal level in the first 10 min during stress. Modulating external glucose and metabolism gate keepers network parameters (GAPDH, G6PDH, TKT), by overexpressing or silencing them, we conclude that the glucose metabolism is supporting the regeneration of antioxidant system and PPP network is thus identified as the main negative feedback in the molecular adaptation here observed.

O16- Bacterial colibactin-induced lipid accumulation and loss of a c-type lectin cooperates for supporting an immune-suppressive microenvironment in right-sided colon cancer

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Right-sided colon cancer (RCC) patients exhibit difference in the microbiota organization in relation to left-sided colon cancer and has a worse prognosis. Among several species of bacteria associated with colon cancer, colibactin-producing by Escherichia coli (CoPEC) are attracting attention. However, if CoPEC contributes to tumor lipid metabolism remains incompletely understood. Herein, we revealed that CoPEC is negatively correlated with human regenerating family member 3 alpha gene (REG3A) expression and trigger reprogramming lipid metabolism, which exacerbates accumulation of glycerophospholipids. Notably, APC mutation and metabolic consensus molecular subtype (CMS3) are predominant in RCC, especially in patients colonized by CoPEC. While SFRP2 expression is increased in these tumors, CD8+ T cells were reduced. In addition, human tumors have similarities to mice tumors. In particular, mRNAs encoding immunoglobulins heavy chains were clearly increased in both models with low Reg3A expression. Taken together, CoPEC associated with REG3A is promising as a biomarker in cancer therapy.

P29 - Space respiratory capacity metabolic biomarker predictive of response to treatment for acute myeloid leukemia

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Acute myeloid leukemia (AML) is a group of hematological malignancies characterized by the clonal expansion in the bone marrow of blood cell precursors blocked at an early stage of differentiation, leukemic blasts. Diagnosis and monitoring of the disease are based on various biological and biochemical examinations of blood blasts and bone marrow. AML are aggressive blood diseases with a 5-year survival rate of 24%. This poor survival can be explained by the fact that even if 2/3 of patients initially respond to treatment, most of them will eventually relapse. The therapeutic choice is based on the evaluation of cytogenetic and molecular criteria which leads to the classification into prognostic groups identified according to the recommendations of the ELN. This stratification has limitations. To improve its predictability, new complementary biomarkers must be characterized. After exposure to conventional treatments, survival of persistent leukemia cells is supported primarily by mitochondrial energy metabolism. Assessing the activity of mitochondria in patient blasts could provide predictive information on the response to treatment. We can use a functional analysis of mitochondrial metabolism, through the measurement of oxygen consumption (Oximetry: Seahorse®). The respiratory chain of mitochondria rarely works at its maximum; it has a reserve allowing it to increase its activity during episodes of energy stress: Spare Respiratory Capacity (SRC). Our team was able to show that SRC was correlated with survival and that it could distinguish 2 populations: High and Low SRC. Patients with Low SRC blasts have a poorer prognosis compared to those with High SRC.

P30 – Adaptation : from molecular dynamics in single cells to organs on-a-chip approaches

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In a changing environment, adaptation is a must condition for a living system to survive. Here we are presenting adaptation as a time dependent process.

In a first approach, we are asking how cells are adapting to anticancer therapies which are exploiting oxidative species. To answer this, we are monitoring breast cancer cells responding to specific oxidative stress, as singlet oxygen or hydrogen peroxide. Singlet oxygen is created via direct transition of O2, upon light stimulation, λex = 1273 nm [1]. 1-4h before irradiation, the intra/extracellular concentration of glucose is increased. Cells are exposed to the same dose of irradiation and their response is quantified 24h after, as cell survival or death. We notice various cell death types and 2 types of responses: higher sensitivity to stress when cells receive stimulation during metabolic networks regulation comparing to cells adapted more than 2h before stress to their new metabolic condition. Here the question arises: what is the interplay between metabolism and oxidative stress? Trying to quantify this transient cellular response, we designed an optofluidic system to observe adaptation at molecular level, in single living cells, with high throughputs [2].

In a second approach we ask how vascular targeting therapies can be exploited to treat tumours. It is well known that blood vessels are adapting, favouring the tumour growth [3]. Our experimental approach is to build in vitro human blood vessels in a biocompatible matrix. We design µfluidic chambers in PDMS and use a sacrificial template approach, to form a perfused, stable blood vessel using primary human endothelial cells. Cells are grown in a proprietary matrix which makes a controlled 3D environment. As perspective, we wish to recreate a tumour in this matrix and perfuse it through the established blood vessel.

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P31 - Role of CD36 in breast cancer metastatic processes

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Breast cancer is the leading cancer in terms of incidence and mortality in women. Breast tumours develop in a complex microenvironment whose main component is adipose tissue. The degree of invasion of the adipose tissue by tumour cells reflects their aggressiveness. We have previously shown that breast mammary adipocytes promote the aggressiveness of breast tumour cells through the overexpression of CD36. CD36 is a long-chain fatty acid transporter that has been shown to play a role in metabolism as well as in tumour aggressiveness in many cancers. Our hypothesis is that CD36 is a potential signature of cancer cells with the ability to metastasize.

Thus, our aim is to determine the molecular mechanisms conferring metastatic potential to breast tumour cells upon overexpression of CD36. To this end, we generated stably overexpressing CD36 clones from two breast cancer cell lines with different molecular subtypes and aggressiveness. In order to study the regulation of lipid metabolism in breast tumour cells according to CD36 expression *in vitro*, we treated our different cell lines with saturated and unsaturated fatty acids. Viability tests showed a different sensitivity of our cell lines to different fatty acids. Furthermore, we were interested in the impact of CD36 overexpression on the proliferative capacity of those breast cancer cell lines. An increased proliferation of the clones derived from the less aggressive breast cancer cell line but not the more aggressive breast cell line was observed. By treating our different cell lines with a saturated fatty acid, we showed a decreased proliferation of those cells.

In conclusion our results suggest that breast cancer cell lines according to their phenotypes present different metabolisms as illustrated by their different sensitivities to treatment with different fatty acids and that CD36 overexpression favors the proliferative capacities of the less aggressive cell line.

O17 - Mixture models and variable selection to identify cancer subtypes and biomarkers

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High-throughput "-omic" technologies (genomics, epigenomics, transcriptomics, proteomics, metabolomics, etc.) hold great potential for gaining insights into complex biological processes and for identifying biomarkers that can be used for improved diagnosis and therapeutic interventions. In this talk, I will present unified methods for identifying latent classes and component-specific biomarkers in -omic datasets by combining ideas of mixture models and variable selection. In particular, I will discuss (1) a bi-clustering approach that allows clustering of samples on subsets of variables to uncover cancer subtypes and their associated biomarkers, and (2) an integrative -omic model that uses stochastic partitioning to identify important features and relationships between different -omic data types. I will illustrate the methods on cancer genomic studies.

O18 - Pressure jump for the Cahn-Hilliard equation: an application to tumor growth

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We are interested in quantifying the pressure jump at the interface of the tumor, assmuming it is an incompressible flow. This jump is related to two antagonistic effects: repulsion of cells when the tumor grows and cell-cell adhesion which creates surface tension. To take into account these two effects, we use the Cahn-Hilliard equation. To compute this pressure jump, we also include an external force and consider stationary radial solutions of the Cahn-Hilliard equation. We also characterize completely the stationary solutions in the incompressible case, prove the incompressible limit and prove convergence of the parabolic problems to stationary states. Our results are based on the two articles [1,2].

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O19 - A mathematical model to study the impact of intra-tumour heterogeneity on anti-tumour CD8+ T cell immune response

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Intra-tumour heterogeneity (ITH) has a strong impact on the efficacy of the immune response against solid tumours. The number of sub-populations of cancer cells expressing different antigens and the percentage of immunogenic cells (i.e. tumour cells that are effectively targeted by immune cells) in a tumour are both expressions of ITH.

In this talk, we present a spatially explicit stochastic individual-based model of the interaction dynamics between tumour cells and CD8+ T cells, which investigates the specific impact of these two expressions of ITH on anti-tumour immune response.

The results of numerical simulations of this model qualitatively reproduce experimental observations of successful and unsuccessful immune surveillance. Moreover, they shed light on the impact of these two characteristics on tumour progression independently and together, assessing their influence on anti-tumour immunity in a controlled manner.

P32 - Multivariate functional principal component analysis for stratified data

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Introduction. : We address the problem of performing dimension reduction on cancer data observed on different domains in a case-control or choice-based sampling design context. The aim is to propose a new multivariate principal component analysis approach when the multivariate functional random variables are observed on different domains and the sampling used is under endogenous stratification.

Methods. : The method derives from a direct relationship between univariate and multivariate functional principal component analysis for finite Karhunen-Loève decompositions. We develop several asymptotic properties to tackle the principal component analysis problem.

Results/expected results. : The numerical results on synthetic data and empirical application using cancer cell lines population dataset show that the proposed methodology outperform compare to that ignores the non-random nature of the data.

Conclusion. : This method open an array of potential extensions to other kind of stratified sampling and applications in clustering or supervised learning models where on is interested to estimate

P33 - Mechanistic models and machine learning for survival analysis helps predicting resistance acquisition in metastatic melanoma patients

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Metastatic melanoma is highly resistant to conventional therapies, but particularly sensitive to treatments targeting protein kinases involved in the canonical MAPK signaling pathway. In fact, the MAPK/ERK pathway is an essential intracellular signaling pathway in metastatic melanoma, and the discovery of activating mutations of the BRAF oncogene has opened new therapeutic avenues with protein kinase inhibitors that have however shown insufficient or transient efficacy due to primary or acquired resistance. Our hypothesis is that immediate sensitivity and acquired resistance to inhibitors can be predetermined by biomarkers related to the initial state of intracellular molecular networks.

By using phosphoproteomic data of melanoma cell lines, we built a predictive mechanistic model that mimics the response of MAPK and PI3K/AKT signaling pathways to kinases inhibitors. We developed an original version of the Modular Response Analysis [1] method to describe how the observed metabolic network responds to small perturbations.

An other issue in oncology is the personalization of the treatment to the patient. From the perspective of developing a strategy for adapting treatment to each patient, we believe that it is essential to understand the individual clinical or biological characteristics influencing the treatment outcome.

We use several statistical and machine learning models to predict the progression free disease time of patients from individual characteristics. Multimodal data integration gives us the opportunity to understand the phenomenon globally through the integration of multiple pieces of information, however the main difficulty in this approach lies in choosing how to properly integrate these different data types.

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O20 - Economic consequences of cancer

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With great strides in cancer screening and treatment, many innovations come at financial hardship and may result in growing disparities between those who can afford care and those who cannot. The goal of this presentation is to discuss ways to create balance between innovation and disparities. Globally, spending on oncology drugs is staggering. While the US accounts for much of the spending, other countries spend hefty sums with European nations not far behind the US. Cancer is the leading cause of medical debt in the US with 3 million people owing more than $10,000. Studies show that cancer's financial burden lasts 5 to 6 years after a cancer diagnosis in older adults, many of whom are insured. Moreover, employed cancer survivors make trade-offs between prioritizing their health and work. In my research, patients report that they will miss treatment before missing work, especially if other household members are dependent on them for health insurance and financial support. We further find that patients who continue to work when instead of recovering report poor health even in retirement. I find that after an initial period of work discontinuation, many return to work, but cannot remain long-term or report greater absenteeism. I discuss how to mitigate financial and employment outcomes by improving affordability, limiting disability, and increasing accessibility through policy, partnerships with providers and community organizations, and interventions from drug discovery to health care delivery.

O21 - Willingness to pay or to make a gift as a measure of efficacy of novel cigarette plain pack warnings: a randomized controlled experiment

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In response to the health burden attributable to tobacco, the implementation of the standardized package and the posting of warnings informing about the consequences of tobacco consumption have been evaluated as effective. These evaluations have most often consisted of either declarative or observational work. Work based on behavioral measures is growing but still has some limitations.

Based on this finding, we conducted a controlled experiment in which participants were exposed to new types of health warnings on standardized packages, and the impact of these exposures was measured by the monetary sacrifice that participants were willing to make. By revealing their willingness to pay (act of purchase) or to give (donation) (WTP/G), it was indeed possible to measure the relative efficacy of the warnings in triggering a behavioral response and its intensity.

Our results are twofold: (i) the WTP/G of participants exposed to the plain package with warnings eliciting negative emotions are significantly higher compared to other types of warnings, which confirms the results previously found in the literature; and (ii) the degree of nicotine addiction modifies the willingness to pay of smoking participants: the greater the degree of addiction, the more they will use positive warnings using cognitive dissonance or commitment as psychological levers to initiate change.

Our behavioral measures show promise in evaluating the efficacy of tobacco control tools. The standardized package with health warnings that elicit negative emotions is an effective tobacco control policy. However, it seems to miss an important population target in terms of public health: nicotine-dependent smokers. For these smokers, warnings mobilizing other motivational levers should be implemented.

O22 - Impact of early diagnostic on oesogastric cancer survival.

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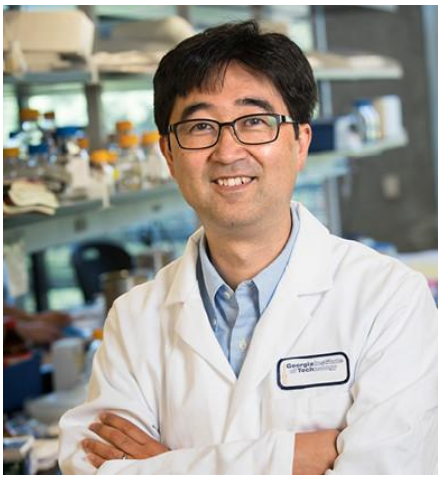
In terms of the incidence of esogastric cancers, France is in the high average of Western European countries. The 5-year survival prognosis is also very poor: between 14% (men) and 18% (women) for esophageal cancers and between 23% (men) and 28% (women) for stomach cancers (INCA, 2019). Overall, gastroesophageal cancers are among the cancers with a poor prognosis. In addition, several studies have shown that excess cancer incidence and mortality may be related to inequalities in terms of behaviors, environmental, socioeconomic and occupational characteristics, but also to inequalities in access to care and prevention, accompanied by strong spatial inequalities (e.g., Observatoire Sociétal des cancers, 2012; INCA 2019): mortality and excess mortality rates are highly contrasted between French departments.

Our project aims to identify the role of the speed of diagnosis (measured by different indicators) of gastroesophageal cancer on the probability of survival (at 3 years), taking into account the socio-economic characteristics of the patient (age, gender, income), but also medical characteristics (such as health status, risk behaviors), and that of the territorial characteristics in which the patient resides or grew up. We use data from the FREGAT database, collected by the Centre Hospitalier Universitaire de Lille, which lists patients admitted to hospital for treatment of esogastric cancer. After cleaning, the database contains about 2000 patients.

Through estimation of econometric survival models, our preliminary results indicate a positive impact of early diagnosis on survival, robust to the definition of the diagnosis and the control variables present in the model. Prompt referral to a general practitioner or specialist after the onset of the first symptoms significantly increases the chances of survival at 3 years.

023 - High-Throughput 3D Cellular Cancer Models



Shuichi TAKAYAMA

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This presentation will describe development of high-throughput (96 and 384 well format) 3D microculture models of breast and other cancers. The presentation will describe some of the underlying engineering technologies and materials science of the platforms along with accompanying biomedical applications of the technologies.

Specific engineering topics to be discussed include:

1. Scaffold-free 3D spheroid cultures, scaffold-rich organoid models, and a recently developed method of minimal Matrigel scaffolding approach to production of geometrically-inverted 3D cell culture models in 384 hanging drop and ultra-low attachment (ULA) plates.

2. Time permitting, microchannel and aqueous two-phase system (ATPS) bioprinting based models will also be discussed including efforts to incorporate stromal cells and immune components.

O24 - Cloud connected medical devices for photoactivated drug delivery

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Founder & CTO at Modulight, Inc.,Tampere, Pirkanmaa, Finland

***Objective*:** There is a continuous need to improve the efficacy of the current cancer drugs and treatments overall. As much as 75% of the approved drugs in the oncology fail to deliver a real impact to the patients' health. Photoactivated drug delivery and photoimmunotherapy are one way of improving the efficacy of cancer drug by improved targeting, local tumor control and inducing long-term immunotherapeutic tumor control.

***Methods*:** We present a family of cloud connected medical laser systems that enable light activated drug delivery, real-time treatment monitoring, and automated data collection and analytics in Modulight.cloud for better efficacy.

***Results*:** We show how a cloud connected medical laser system improves the accuracy and control of the light activated drug delivery by means of monitoring the light delivery and photoimmunotherapy process in treatment of glioblastoma. We also show how such a system provides a generic platform for a multi-component photoactivated drug delivery that can include antibody targeting, locally enhanced chemotherapy combined with photoimmunotherapy.

***Conclusion*:** Our cloud connected medical laser system has a great potential to improve the efficacy of the existing cancer drugs and introduce a well-controlled targeted multi-component treatment modality in oncology. Modulight.cloud platforms further offers the opportunity to continuous efficacy improvement via real-time and post treatment analytics.

O25 - Development of a light emitting device for the treatment of peritoneal carcinomatosis of ovarian origin by intracavitary photodynamic therapy

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Introduction **:** Ovarian peritoneal carcinomatosis (OPC) is an evolution of ovarian cancer defined by dissemination of cancerous cells to the peritoneal cavity. Photodynamic therapy (PDT) has been proposed in complement to the standard of care. However, literature has highlighted the lack of relevant illumination device. In this study, we proposed and assessed several illumination protocols as medical devices to identify the more relevant one.

Methods **:** First, a test bench aiming to evaluate quantity and homogeneity of the delivered illumination has been developed using optical probes connected to powermeters.
Then, four illumination devices were implemented and assessed. The first one consisted of six fixed light emitting fabrics (LEF), the second one was a moving luminous wand, the third one, a hybrid one, combined a fixed luminous wand and six fixed LEF and the last one involved seven luminous balloons.

Results **:** The optical probes received a mean light dose (a variation coefficient) of 1.44×10-1 J/cm2 (119.6%) with the first illumination device, 3.07×10-2 J/cm2 (87.2%) with the second one, 1.47×10-1 J/cm2 (71.7%) with the third one and 6.98×10-1 J/cm2 (40.9%) with the last one. The balloons, which therefore represented the most performant illumination device, unfortunately required many laser sources due to a poor optical yield. Thus, the second most performant device, the hybrid method, represented most relevant illumination device.

Conclusion **:** Illumination solutions for PDT of OPC have been proposed and tested. One solution has been approved. Operating lamp appears to represent environmental condition that could be considered in the calculation of light dose.

O26 – Spidermass : a novel tool for immune score for patient prognosis in ovarian cancer.

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Patient survival of ovarian cancer is closely linked to the precision of surgery, especially in ovarian cancer. As these cancers are diagnosed in late stage, the quality of surgery depends on removing every tumoral cells to avoid any recurrence without damaging healthy tissue. Thus, early diagnosis and molecular information of the tumoral environment is crucial to improve life quality of patients. Thanks to the SpiderMass technology, we are able to perform in vivo analysis able to give in real-time diagnosis of ovarian cancer and prognosis of the patient.

A cohort of 79 surgical piece of ovarian cancer and 68 of endometrium cancer were analyzed by SpiderMass. 92% of good classification was obtained between all the subtypes of cancers. Taking into account the survival of patient, a clear separation has been retrieved between mucinous and serous. We then investigate the macrophages infiltration into the tumor and their phenotype (pro- inflammatory versus pro-tumoral). For that purpose, we identified specific lipids of macrophages and evaluated their tumor infiltration by spidermass and validate by immunofluorescence based on specific markers (Cd206, Inos, Cd86). We cultivate these macrophages under immunosuppressives conditions with Il-4 cytokines and try to identify specific markers. Based on these results, macrophages lipid markers have been tested on the tissue cohort and allowed to find specific abondance according to the subtype of cancer. Interestingly, the intensities of these markers and closely linked with the aggressiveness of the cancers. That's why SpiderMass can be used as a real time ex vivo immune score for patient prognosis through macrophages infiltration determination.

P34 - Multilayered blood vessels-on-chip for high-throughput testing of the vascular barrier.

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Blood vessel-on-a-chip (VoC) aim at reproducing vascular functions. In order to address the challenges of making structurally correct, multicellular VoC using a simple method with the aim of producing large numbers of vessels at a time, we used the viscous finger patterning (VFP) technique which allowed for the making and testing of several tens of blood vessels simultaneously in standard multi-well format suitable for high-throughput drug screening. The devices were fabricated in polydimethylsiloxane and composed of 48 independent rectangular channels. The channels were filled with collagen, then tubes were formed inside using VFP with improvements.

The engineered VoC showed well-structured endothelial cell adherens- and tight-junctions, as assessed by VE-cadherin and actin immunostaining and confocal microscopy. VoC were reactive to pro-inflammatory cytokines (TNFα, IL-1) and to permeability agonists (thrombin). A double-VFP approach was used to create more complex and structurally correct vessels by consecutively seeding perivascular and then endothelial cells in concentric and distinct layers. The addition of perivascular cells greatly improved the VoC barrier functions. A permeability assay was designed, and a method was setup to calculate diffusive permeability coefficients from video recordings of the diffusion of fluorescent dextran. The devices allowed the recovery of nucleic acids from each single vessel for transcriptomic analyses. Furthermore, the design allowed the making and use of tens of vessels in parallel, which could be challenged with biological replicates in different conditions, including positive and negative controls at the same time, making the process compatible with medium- to high-throughput screening.

References

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P35 - Mechanical characterization of single cells during intracellular visualization

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Biophysical signatures of a cancer cell, such as mechanical properties, have a critical role in the cell functionality. Several studies have shown the link between the mechanical response of the cell and the intracellular components. However, there is no method to evaluate the effect of subcellular elements on the mechanical response of the cancer cell.

To integrate mechanical characterization with subcellular visualization, we combined two independent parts: the measurement part and the visualization part. The measurements were performed by MEMS Tweezers integrated with a microfluidic device on a confocal microscope stage to visualize intracellular components simultaneously. We used SUM159PT, a triple- negative breast cancer cell line and nuclei were stained with NucBlueTM nuclear staining (Invitrogen), and Tubulin with 488 Taxol. To characterize the single-cell, we injected a cell suspension into the inlet of the microfluidic channel and flowed it through the channel with a pressure pump connected to the outlet of the channel. Then, a MEMS "hand", capable of moving in 3 directions with submicron accuracy, captured a single cell and performed a compression assay to obtain mechanical properties, *e.g.*, stiffness and viscosity. The real-time confocal imaging provided information on the position and structure of subcellular elements during the mechanical characterization to evaluate the effect of subcellular components on the mechanical response of a cancer cell.

In short, we developed a method capable of performing simultaneous subcellular imaging and mechanical characterization of single cancer cells to create a link between the mechanical response of the cell and its subcellular elements.

P36 - Single-cell pairing in a microfluidic device for immunological synapse monitoring

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Monitoring cell-cell interaction through an immunological synapse (IS) requires cell pairing at the single-cell level. Single-cell pairing remains challenging for primary cancer research due to cell size heterogeneity between immune and leukemic cells, and availability in limited numbers. Typical approaches, e.g., dish-based co-culture systems and poly-L-lysine coated coverslips, provide neither controlled nor well-defined pairing, resulting in poor early cell- cell interaction monitoring. Several microfluidic devices, using physical cell traps, offer well- controlled cell pairing but suffer from pairing cells of different dimensions. Thus, a practical method, suitable even for a limited number of cells having significantly different dimensions, is needed. To fill this gap, we demonstrate a practical and stable method for pairing cells of different dimensions even for a low number of cells.

The method targets single T-lymphocyte and leukemic cell synapse formation, allowing fluorescent observation of early or later cellular events. Hydrodynamic flow focusing in the z-direction can modulate the effective channel height for efficient cell capturing. The results showed a successful single-cell pairing of ~70% (for >300 traps/device). Due to the sensitivity of immune cells to pressure changes, stability is ensured by providing constant flow in the analysis area. Finally, we monitor the activity of primary T-lymphocytes during formed synapses with leukemic cell lines (KG1) and blasts from AML-suffering patients. The activity was monitored by $Ca2_+$ imaging with a ratiometric dye (Fura-2/AM) observed by fluorescence microscopy.

To conclude, the proposed method is a promising tool for performing functional studies at the IS level to investigate the diversity of malignant cell behaviors.

P37 - Development of a microfluidic system to study tumor-stroma interactions and drug sensitivity

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Introduction. During their growth and development, tumors generate physical forces, creating mechanical cues including extracellular matrix (ECM) rigidity, compression stress and shear stress. These mechanical cues can activate signaling pathways involved in tumor aggressiveness, and can increase tumor chemoresistance, therefore reinforcing the need for accurate tumor model for drug screening. Microfluidic systems have been increasingly used to fabricate tumor-on- chips to better imitate in vivo cancer models by giving a greater control over culture conditions by including physical characteristics such as shear stress or compression.

Methods. A polydimethylsiloxane (PDMS) microfluidic device was fabricated using 3D printed molds. The device is separated into two parts: a bottom part and a closing cap, allowing easier access to the biological sample as well as enabling different channel heights. To realize a leakage proof closure of the system, aluminum plates are screwed on each side of the system.

Results. The fabrication protocol was developed and optimized to reduce the time of fabrication by using 3D printing to create PDMS molds. The molds were designed to create a PDMS chip with open channels as well as a cap with adjustable depth. A measuring system was incorporated to precisely measure the height of the channel once closed using two aluminum plates. These plates were milled to allow optical observation of the system during culture.

Conclusion. A new fabrication process was optimized to increase the ease of use of a microfluidic system whilst enabling the addition of key tumor features to further understand the mechanism of chemoresistance.

P38 - Révélation de profils lipidiques spécifiques du cancer œsogastrique par imagerie MALDI-MSI et SpiderMass

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Introduction **:** Avec 1 million de cas par an, le cancer œsogastrique (CE) est le cinquième cancer le plus diagnostiqué dans le monde. Le CE englobe plusieurs types d'adénocarcinomes, comme les types tubulaires, mucineux et les PCC, ces derniers comprenant 2 sous- types, SRC et NOS. Le PCC est un type agressif, survenant chez des patients jeunes, et extrêmement difficile à diagnostiquer en raison de son caractère diffus. En particulier, pendant les examens extemporanés, conduisant à une rechute d'environ la moitié des patients. L'objectif est de mettre en place un diagnostic peropératoire plus spécifique pour guider le geste des chirurgiens dans l'ablation de la tumeur entière en se basant sur une technologie de spectrométrie de masse, le SpiderMass.

Résultats **:** La cohorte de 146 échantillons de CE a été analysée par MALDI-MSI dans les deux polarités. Les analyses multivariées révèlent que chaque type et sous-type de CE présente un profil moléculaire différent et spécifique permettant une discrimination nette. Les marqueurs discriminants ont été identifiés par MS2 et annotés manuellement. Il est intéressant de noter qu'une hétérogénéité moléculaire importante est révélée par MALDI-MSI pour les tissus sains et cancéreux. En raison de la forte similitude entre les spectres MALDI et WALDI (93%), la même cohorte a été analysée par la technologie SpiderMass. Les données SpiderMass ont ensuite été utilisées pour construire des modèles de classification pour le typage et le sous-typage des CE. Les modèles de classification seront ensuite validés en aveugle pour ensuite être déployés en condition réelle pour comparer les performances par rapport à celle de l'anatomopathologiste.

P39 - Development of a microfluidic flow system for the dynamic perfusion of blood vessels-on-chip

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During cancer progression, the formation of new blood vessels is a major process which favors tumor growth and metastatic dissemination, leading to therapeutic failures. The recent development of organs-on-chips (OoCs), that combine new advances in tissue engineering and in microfabrication, allow to investigate human cellular functions and physiopathological processes; these have gained great interest for fundamental research by providing more relevant in vivo 3D models while reducing the need for animal testing. The laboratory has previously developed a blood vessel-on-chip model using the viscous finger patterning (VFP) technique (Delannoy et al., 2022); the microfabricated vessels consisted of a microchannel made of collagen with a controlled-inside diameter, and coated with endothelial cells, reproducing an established blood vessel. This work aims to develop a microfluidic system allowing to obtain a steady-flow perfusion of these blood vessels-on-chip. Our set-up is based on the control of the laminar flow by applying negative pressure, for optimizing the flow stability. Tubing components (length and diameter) were defined in order to set the hydraulic resistance of the system and to apply a physiological shear-stress to cells. The system was calibrated by measuring the shear-stress depending on the flow rate applied. The initial experiments using this configuration indicated that cells were not damaged by the steady-flow during the perfusion time. This system allows to maintain cultured-endothelial cells in a more physiological environment than static culture. The next step of this work is to characterize the cellular physiology under these dynamic conditions, such as cell orientation and endothelium functionalities.

P40 - Functional study of calcium homeostasis in residual leukemic cells in acute myeloid leukemia : contribution of micro-fluidic

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The minimal residual disease (MRD) observed in acute myeloid leukemia (AML) is due to the persistence of a small number of leukemic cells that escape chemotherapy. As relapses are frequent, it is crucial to characterize these residual leukemic cells (RLC). A recent publication from the laboratory showed *in vitro* the under-expression of the ORAI1 calcium channel in patient leukemic cells, and its involvement in the quiescence of chemo-resistant cells with stem cell properties. Our goal is to explore AML RLC calcium signature, starting with the potential role of ORAI1 channels in these cells.

Persistent AML patient RLC in PDX (Patient Derived Xenograft) mice, an MRD model developed by the lab, were sorted by FACS and used to analyze calcium homeostasis (ORAI1 calcium channel activity). Because of the small number of cells, microfluidic devices will be used to capture them and analyze their calcium flux in real time. These responses have been characterized with the injection of pharmacological modulators of calcium channels. Analysis of channel expression and NFAT (Nuclear Factor of Activated T cell) isoforms has also been performed by qPCR.

According to our results, human RLC from the MRD model appear to have altered calcium homeostasis.

P41 - Including the matricial tumoral microenvironment in 3D in vitro models by using a Hyaluronic-Acid-based hydroscaffold™

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In oncology, 97% of drug candidates fail in clinical trials. This highlights a lack of relevance of preclinical models used upstream. Indeed, human *in vitro* models don't consider the Tumoral Extracellular Matrix (TECM). However, more and more studies demonstrate that ECM composition and stiffness are modified in tumors and are linked to cancer initiation, progression, propagation, and drug resistances.

BIOMIMESYS® is a Hyaluronic Acid-based matrix grafted with structural and adhesion molecules, which mimics the ECM/TECM. It is chemically defined and its composition and stiffness can be modified to reproduce the organ-specificity of the ECM, or to mimic a pathological microenvironment *in vitro*.

We have demonstrated that the exposition of colon cancer cells cultured in BIOMIMESYS® *Oncology* matrix to an anti-proliferative drug showed a closer *in vitro/in vivo* correlation in the EC50 curve compared to 2D culture. Cancer cells can be advantageously grown in BIOMIMESYS® for several weeks in multiwell plates and in microfluidic chips for more advanced models. We also observed that modifications in the matrix composition and stiffness modify the cell behavior. Moreover, thanks to collaborations with academic laboratories, we demonstrated that BIOMIMESYS® allows to reproduce *in vitro* the behavior of cancerous cells *in vivo*, like mutation effects and metastasis propagation, and could be a relevant alternative to animal models.

These results showed that the matricial microenvironment modifies the cell behavior *in vitro* and should be considered carefully in drug discovery. BIOMIMESYS® *hydroscaffold*TM is adapted to High Content Screening and represented a powerful tool to better select drug candidate.

O27 - Why (and how) we should care about Quality of Life in childhood cancer

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Although with disparities, pediatric cancer care has been particularly successful at saving lives. Thisraises new questions on short- and long-term vulnerabilities due to toxicities on the developing body. In this talk, I will insist on the toll of health risks on Quality of Life (QoL).

First, I will draw on the results of the PÉTALE project which recalled 250 survivors of childhood Acute Lymphoblastic Leukemia (cALL) from Québec (median age 22 years, CHU Sainte-Justine). This project demonstrated early vulnerabilities across different domains including cardiometabolic health, cardiac function, and psychosocial well-being. Results yielded a refined description and detection strategies in multiple spheres (e.g. psychosocial, neurocognitive) and pointed to new targets and a family approach for interventions.

Second, I will present how the identified challenges were addressed in a new healthy lifestyle promotion intervention named VIE after “Valorization Implication Education”. It is an intensive multi-component intervention in preventive medicine, including nutrition counseling, physical activity training, and psychosocial support, and is typically implemented during treatments. Thepsychosocial support component calls for problem-solving skills training and family resilience reinforcement. I will present encouraging results and challenges on feasibility of this component. VIE has clear potential to impact health, but before we can prove it, we need to increase intervention capacity and refine the intervention format-content for subgroups. This integrated health approach illustrates the new roles of psychosocial and behavioral scientists in pediatric oncology.

O28 – Digital health interventions to support cancer patients and caregivers : what works? For whom? An umbrella review.

Kristopher Lamore[1], Christelle Duprez[1], Delphine Grynberg[1], Pascal Antoine [1], Valentyn Fournier[1]

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***Objective*:** From an almost exclusively institutionalized care, patient care moved to more outpatient care. This care paradigm shift leads to a new reflection on how to adequately support patients and caregivers. In this context, numerous digital interventions have been developed to support cancer patients and caregivers. Hence, an umbrella review was conducted to identify (1) what are the digital interventions developed to provide supportive care (psychological support, physical activity, pain management, etc.) to cancer patients and their relatives, and (2) the effect or effectiveness of these interventions.

***Methods*:** Systematic reviews and meta-analyses of intervention research evaluating the effect or effectiveness of supportive care interventions using a web-based or mobile-based design offered to cancer patients and their relatives were identified from 2000 to 4th April 2022. Searches were made on CINAHL, Cochrane Library, EMBASE, PubMed and PsycINFO databases.

Results: Eighteen studies were identified according to eligibility criteria. Most interventions used a web-based design targeting behaviors (physical activity, tobacco, or alcohol use) or emotions (positive and negative affect, emotional management). Interventions targeting functional outcomes (e.g., pain, fatigue) or quality of life were also retrieved. Significant and positive results were observed for functional and quality of life outcomes, while mitigated results (positive or no effect) were identified for behavioral and emotional outcomes. Only one systematic review focused on caregivers.

Conclusion: The results of this umbrella review are still in progress. However, this work allows to develop an innovative digital intervention, considering the benefits and limitations of the existing tools, and to formulate recommendations.

O29 - Raising the physicians' awareness regarding Young Carers in oncology: an interventional research

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Objective: Many children and adolescents who are confronted to a relative with cancer, may also provide regular and significant support at home. They are called Young Carers (YCs). This situation provokes many consequences for the youth, who frequently need help from healthcare professionals. However, YCs would not be identified by these professionals. To support YCs, it is essential that healthcare professionals are aware of and able to identify these youth. As primary patient contacts, physicians would be in the best position to identify YCs. Thus, this study aims to investigate the knowledge, the attitudes, and the practices that physicians in oncology have about YCs.

Methods: 120 physicians and 275 others healthcare professionals in oncology took part to an online survey. They reported socio-demographic and professional information, their knowledge and experience with YC, and their personal experience as a carer.

Results: Descriptive and comparative analyses are in progress to investigate differences between physicians and the others professionals, as well as intra-category analyses to identify factors influencing physicians' attitudes and practices.

Conclusion: It is essential that each professional become aware of the existence of YCs, so that they can identify them among their patient's relative and refer them to appropriate resources with the departments. Better understand the specificities and the level of awareness of each professional, notably the physicians, will allow the development of appropriate training to increase their knowledge and improve their ability to identify and support YCs and their families.

Keywords: cancer; physicians; practices; professional support; young carers

O30 - Improving emotion regulation in breast cancer patients in the early survivorship period : Efficacy of a brief ecologically boosted group intervention

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Purpose : This study reports the primary short- and mid-term benefits of an eight-session ecologically boosted emotion and self-regulation group intervention designed for breast cancer patients in the early survivorship period meeting criteria for clinical levels of psychological symptoms.

Methods : Patients were randomly assigned to the immediate intervention arm (*n*=61; intervention received immediately after radiotherapy had ended) or to the delayed intervention arm (*n*=59; intervention received five months after radiotherapy had ended). Emotion regulation was assessed in a dynamic emotion regulation task and in everyday life. Psychological symptoms, including anxiety, depressive symptoms, fear of cancer recurrence (FCR), intrusive thoughts, and worry, were assessed through questionnaires. Assessments were completed at baseline (T1), five months (T2) and ten months (T3) later.

Results : Patients from both arms improved their ability to regulate the intensity of their negative emotions when exposed to cancer-related triggers in the dynamic emotion regulation task. They reported lower levels of emotional distress, intrusive thoughts, and worry. These benefits were maintained five months later at the mid-term follow-up. Benefits for everyday life emotion regulation were observed for the immediate intervention arm only, in which patients reported more positive emotions in the short-term.

Conclusions : The intervention improved emotion regulation and psychological symptoms in breast cancer patients in the early survivorship period meeting criteria for clinical levels of psychological symptoms. The small effect sizes suggest that breast cancer patients may benefit from consolidation sessions to sustain the benefits and to reinforce the transfer of emotion regulation skills in their everyday life.

US Clinical Trials Register NCT03336827

P42 - Hypnosis, meditation, and self-induced cognitive trance to improve post-treatment oncological patients' quality of life.

Charlotte Grégoire[1], Nolwenn Marie[1], Corine Sombrun[2], Marie-Elisabeth Faymonville[3], Ilios Kotsou[4,5], Valérie Van Nitsen[4], Sybille De Ribaucourt[4], Guy Jerusalem[6], Steven Laureys[7,8], Audrey Vanhaudenhuyse[1], Olivia Gosseries[9]

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Introduction: Cancer-related fatigue (CRF), emotional distress, sleep difficulties and pain are commonly reported in oncology. Interventions based on non-ordinary states of consciousness (NOCs), mostly hypnosis and meditation, showed first benefits on these symptoms. Self-induced cognitive trance (SICT) is another NOC, inherited from traditional shamanic practice, that may also have therapeutic applications in oncology. Previous case studies reported subjective experience of pain decrease and strength increase during SICT. Investigating its clinical applications, along with hypnosis and meditation, could help improving available therapeutic options in oncology.

Objectives: This preference-based longitudinal controlled trial aims to (1) evaluate the short- and long-term benefits of hypnosis, meditation, and SICT on CRF, emotional distress, sleep difficulties, and pain in patients with cancer; (2) measure the evolution of phenomenological and neurobiological correlates of these three interventions; and (3) confirm the biopsychosocial model of hypnosis and investigate the mechanisms of action of meditation and SICT.

Methods: Questionnaires, free recall recordings and neurobiological measures (i.e., EEG, EMG, ECG, respiration, body temperature, tumor markers rate) will be collected before the intervention, immediately after the intervention, and at 3- and 12-month follow-up. Preliminary data will be presented at the congress.

Discussion: There is a growing interest from patients with cancer in complementary approaches, such as hypnosis, meditation, and SICT. This study will be useful to increase knowledge about short- and long-term effectiveness of 3 group interventions for CRF, emotional distress, sleep, and pain. It will also allow a better understanding of the phenomenological and neurobiological correlates of these 3 NOCs.

P43 - Maladies chroniques et bien-être sexuel : une revue parapluie de la littérature

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Contexte/Objectifs : Les maladies chroniques (MC) sont prises en charge par le corps médical et le bien-être du patient est questionné, mais leurs conséquences sur la sexualité sont encore souvent sous-évaluées et insuffisamment prises en charge. Nous savons que vivre avec une MC peut modifier les fonctions sexuelles et corporelles. Ces modifications ont un effet sur la qualité des relations affectives et sexuelles du malade, mais également sur le partenaire.

Méthodes : Nous avons sélectionné les revues existantes sur les troubles sexuels (TS) et les MC concernant un public d'adulte via 6 bases de données (Embase, Scopus, PubMed, PsycInfo, Cochrane et Cinahl). Nous avons sélectionné les MC physiques sur base de la liste de la platforme ComPaRe et exclu les psychiques, gynécologiques, urologiques, ainsi que les cancers des zones sexuées du corps, vu leur impact évident sur la sexualité.

Résultats : 35 revues ont été incluses reprenant 1 303 906 patients. Chez la femme, le désir, l'excitation, la lubrification, l'orgasme et la satisfaction diminuent alors que la douleur pendant les rapports sexuels augmente dans 8 des 13 MC. Chez l'homme, la dysfonction érectile est le plus couramment signalé dans 10 des 13 MC ; l'anxiété et la dépression comptent pour 6 MC sur 13.

Discussion : Cette étude est encourageante et démontre la nécessité de poursuivre les recherches sur les effets des MC sur la sexualité, dans le but d'améliorer la prise en charge.

Mots clé : Dysfonctions sexuelles, maladies chroniques, troubles sexuels, revue de revues

P44 - The Colofight feasibility study : Hypnosis and Cognitive Behavioral Therapy with online sessions to reduce fatigue in patients undergoing chemotherapy for a metastatic colorectal cancer

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Background : This study aims to implement two interventions (CBT and hypnosis) for the management of cancer-related fatigue. Although CBT is known to be effective in treating cancer-related side effects, it requires specific training often reserved for psychologists. On the other hand, hypnosis has the advantage of being increasingly practiced by caregivers and is therefore less expensive, but it is more difficult to standardize. Implementing an intervention in a healthcare setting is complex and recruiting participants can be challenging. Thus, we aim to evaluate the feasibility of implementing this type of intervention.

Methods and design : A prospective, single-center, randomized interventional feasibility study, using mixed methods (both quantitative and qualitative). 60 patients will be randomized and allocated to each intervention group (Hypnosis (n=30) and CBT (n=30)). Both programs will consist of 6 weekly sessions focusing on the fatigue management over a period of 6 weeks. Trained therapists will conduct the program combining 3 face-to-face sessions and 3 online sessions. The feasibility and experience of interventions will be evaluated by qualitative interviews. Quality of Life and daily fatigue will be self-assessment using an online application from the cancer center.

Discussion : Inclusions are ongoing but the oral presentation could focus on the overview of the two interventions and in particular how the authors standardized the hypnosis sessions. Specific exercises are proposed to target the determinants of fatigue (eg. distress). The next step in this project is the opening of a multi-center RCT. An opportunity to discuss with clinicians and researchers interested in the interventions.

P45 – FREGAT : the clinico-biological database dedicated to esophageal and gastric cancer

Stéphanie Devaux[1], Antoine Adenis[2], Florence Renaud[3], Guillaume Piessen[4], the FREGAT working group

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While the incidence of esophageal and gastric cancers is increasing, the prognosis of these cancers remains bleak. Multimodal treatments, associating chemotherapy, targeted therapies, immunotherapy, radiotherapy, surgery and endoscopy are needed for the vast majority of patients who present with locally advanced or metastatic disease at diagnosis. Although survival has improved, most patients still present with advanced disease at diagnosis. In addition, most patients exhibit a poor or incomplete response to treatment, experience early recurrence and have an impaired quality of life.

The prospective FREGAT database, established by the French National Cancer Institute, is focused on adult patients with esophageal and gastric carcinomas and on whatever might be the tumor stage or therapeutic strategy. The database includes epidemiological, clinical, and tumor characteristics data as well as follow-up, human and social sciences quality of life data, along with a tumor and blood bank. The mian objective of the database is to identify patients, biological and tumoral factors associated with resistance to antitumoral treatment. Since 2014 more than 5 100 patients are included in FREGAT divided into 35 french centers. Patients are included at the diagnosis of the esogastric cancer. Each patient is followed-up for 5 years. From the database a diversity of scientific project allows to carry out fundamental, translational and clinical studies. 8 publications have already been produced with currently 25 projects. The aim of this poster is to present the most relevant projects in order to favor future collaborations inside and outside ONCOLILLE.

P46 - Evaluating the role of positive traits and states on mortality in cancer : preliminary results from a systematic review and meta-analysis

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Traditionally, the literature investigating psychological factors in relation to cancer mortality focused on negative factors such as depression or distress. This field has produced many studies; results from such studies have now been compiled in meta-analyses which allowed for the clear identification of risk factors (e.g., depression is significantly predictive of mortality in cancer patients). Nevertheless, positive psychological factors (states or traits) might be as crucial regarding cancer mortality but have been neglected. However, while less numerous, studies in this domain have been conducted and have produced mixed results. A meta-analysis was thus needed to shed light on this field.

Therefore, we conducted a systematic review and meta-analysis aimed at identifying the positive states and traits linked to mortality in cancers. Four databases (Pubmed, PsycINFO, Embase, and the Cochrane Library) were searched in order to find longitudinal studies linking positive states and traits to mortality in cancers. Two reviewers completed each stage of the study selection process, the data extractions and the risk of bias assessments. Twenty-six studies involving 822 965 patients were included based on the 2462 references identified.

The meta-analysis conducted on these studies reveals that positive states and traits are predictive of decreased cancer mortality (e.g., studies based on HR: $HR_{random} = .895$ [.86, .93], $z = -5.34$, $p < .001$). Well-being, optimism or vitality might thus be protective against mortality in cancers.

This work emphasizes the need to consider patients with cancer in their globality, including their psychological well-being to provide the most favorable conditions for survival.

P47 - Generic and health-related conspiracy beliefs decrease intention to use chemotherapy : two pilot studies

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Conspiracy beliefs (CBs) imply deleterious effects on intake of particular treatments such as conventional medicine [CM] or non-conventional medicine [NCM]. Yet, the use of NCM as a complement or an alternative represents a crucial health problematic. Indeed, it is linked with a poorer prognosis in cancer patients (Johnson et al., 2018). Only few studies investigated the relations between CBs and medication intake in oncology. The aim of this research is to investigate the links between generic and chemotherapy-specific CBs and intention to use CM and NCM in two hypothetical scenarios studies proposed to general population.

In study 1, after answering to questions relative to generic CBs and chemotherapy-specific CBs, participants were asked to put themselves in the shoes of a cancer patient treated by chemotherapy. Finally, intention to use CM or NCM were measured. General conspiracy beliefs are negatively linked with intention to use CM ($\beta = -.40$; $p < .001$) and positively with the use of NCM in complement ($\beta = .19$; $p < .01$) and as an alternative ($\beta = .44$; $p < .001$). Those links are fully mediated by the chemotherapy-specific CBs.

Study 2 replicates these results and suggests that the effects of generic conspiracy beliefs are best explained by adherence to CBs challenging groups perceived as economically powerful, including pharmaceutical companies.

These results are discussed emphasizing the importance of: (a) replicating these findings in a cancer patients population; (b) developing evidence-based interventions to prevent and reduce the effects of CBs among cancer patients.

ORAL PRESENTATIONS

***O1 - Targeting multidrug resistant cancer- an unfinished business*. Gergely SZAKACS**

O2 - Neurotrophins promotes brain metastasis of triple negative breast cancer through Src kinase family activation. Julien Cicero, Sarah Trouvilliez, Martine Palma, Gaetan Ternier, Laurine Decoster, Nicolas Barrois, Lucie Dehouck, Eloise Happernegg, Roland Bourette, Eric Adriaenssens, Chann Lagadec, Cagatay Mehmet Tarhan, Dominique Collard, Zied Souguir, Elodie Vandenhaute, Grégory Maubon, Nathalie Maubon, François Sipieter, Nicolas Borghi, Paolo Giacobini, Vincent Prevost, Fabien Gosselet, Xuefen Le Bourhis, Isabelle Van Seuningen, Caroline Mysiorek and Robert-Alain Toillon.

O3 - Development of tools for spatio-temporal analysis of phenotypic dynamics of breast cancer cells. Mathilde Brulé; Marie Denoulet; Anaïs Horochowska; Flavie Woesteland; Xuefen LeBourhis; François Anquez and Chann Lagadec

O4 - Modulation of senescence-associated mechanisms in cancer therapy. Marco Demaria

O5 - Deciphering the PD-1/PD-L1 calcium signature in the immunological synapse : microfluidic single cell technology towards precision immunotherapies. Clara Lewuillon, Aurélie Guillemette, Faruk Azam Shaik, Nathalie Jouy, Carine Brinster, Dominique Collard, Bruno Quesnel, Mehmet Cagatay Tarhan, Loïc Lemonnier, Yasmine Touil

O6 - In Vitro Study of the Role of TRPM7 Kinase in Metastatic Mechanisms of Pancreatic Cancer Cells. Julie Auwercx, Alison Vanlaeys, Frédéric Hague, Isabelle Dhennin-Duthille, Philippe Kischel, Bernadette Neve, Halima Ouadid-Ahidouch, Isabelle Van Seuningen, Nicolas Jonckheere, Mathieu Gautier

***07 - Altered glycosylation in cancer: dissecting the molecular mechanisms and understanding the clinical implications*. Celso REIS**

08 - In search of the best antibody format for immune checkpoint inhibitors. Hervé WATIER

O9 - Role of Galectin-9 in the Induction of Tolerogenic Dendritic Cells Mediated by Nasopharyngeal Carcinoma Exosomes. Camille Trioen, Anthony Lefebvre, Guillaume Grolez, Pierre Busson, Olivier Moralès, Nadira Delhem

O10 - IL-2 is inactivated by the acidic pH environment of tumors enabling engineering of a pH-selective mutein. Silvia Gaggero, Jonathan Martinez-Fabregas, Adeline Cozzani, Paul Fyfe, Malo Leprohon, Jie Yang, F. Emil Thomasen, Hauke Winkelmann, Romain Magnez, Alberto G. Conti, Stephan Wilmes, Elizabeth Pohler, Manuel Van Gijsel Bonnello, Xavier Thuru, Bruno Quesnel, Fabrice Soncin, Jacob Piehler, Kresten Lindorff-Larsen, Rahul Roychoudhuri, Ignacio Moraga, Suman Mitra

***O11 - Machine learning and multi-omics approaches for the description and modelling of the tumour microenvironment*. Vera PANCALDI**

O12 - Classification of single cancer cells based on their biophysical signatures. Bahram Ahmadian, Deborah Mbujamba, Jean-Claude Gerbedoen, Hua Cao, Dominique Collard, Sophie Dabo-Niang, Chann Lagadec and Çagatay Tarhan

O13 - High-throughput biophysical analysis of single cells. Quentin Rezard; Marie Denoulet; Faruk Azam Shaik; Jean Claude Gerbedoen; Fabrizio Cleri; Dominique Collard; Chann Lagadec and Mehmet Çagatay Tarhan

O14 - Rest energetic assessment and sensitivity to immune checkpoint inhibitors in oncology. **François GOLDWASSER**

O15 - Adaptation of breast cancer cells : variability of single cells responses. Dana SIMIUC, Francois ANQUEZ, Quentin THOMMEN, Benjamin PFEUTY, Emmanuel COURTADE

O16- Bacterial colibactin-induced lipid accumulation and loss of a c-type lectin cooperates for supporting an immune-suppressive microenvironment in right-sided colon cancer. Nilmara de Oliveira Alves, Amaury Vaysse, Guillaume Dalmasso, Darja Nikitina, Olivier Boulard, Thomas Paz Del Socorro, Pierre Sauvanet, Lionel Poulin, Sean Kennedy, Iradj Sobhani, Richard Bonnet, Mathias Chamaillard

O17 - Mixture models and variable selection to identify cancer subtypes and biomarkers. **Mahlet TADESSE**

O18 - Pressure jump for the Cahn-Hilliard equation: an application to tumor growth. Charles Elbar, Benoît Perthame, Alexandre Poulain, Jakub Skrzeczkowski

***O19 - A mathematical model to study the impact of intra-tumour heterogeneity on anti-tumour CD8+ T cell immune response*.** Emma Leschiera ; Tommaso Lorenzi, Shensi Shen, Luis Almeida, Chloé Audebert

O20 - Economic consequences of cancer **Cathy BRADLEY**

O21 - Willingness to pay or to make a gift as a measure of efficacy of novel cigarette plain pack warnings: a randomized controlled experiment. Christian Ben Lakhdar, Antoine Deplancke, Fabrice Le Lec, Sophie Massin, Anthony Piermatteo, Nicolas Vaillant

***O22 - Impact of early diagnostic on oesogastric cancer survival*.** Nicolas Debarsy, Anne-Laure Samson, Camille Auxépaules

023 - High-Throughput 3D Cellular Cancer Models. Shuichi TAKAYAMA

O24 - Cloud connected medical devices for photoactivated drug delivery. **Petteri UUSIMAA**

O25 - Development of a light emitting device for the treatment of peritoneal carcinomatosis of ovarian origin by intracavitary photodynamic therapy. Laurine Ziane, Grégory Baert, Pascal Deleporte, Olivier Morales, Léa Boidin, Anne-Sophie Vignion, Nadira Delhem

O26 – Spidermass : a novel tool for immune score for patient prognosis in ovarian cancer. Roussel Lucas, Robin Yves-Marie, Lemaire Anne-Sophie, Narducci Fabrice, Salzet Michel, Fournier Isabelle

***O27 - Why (and how) we should care about Quality of Life in childhood cancer*. Serge SULTAN**

***O28 – Digital health interventions to support cancer patients and caregivers : what works? For whom? An umbrella review*. Kristopher LAMORE**

O29 - Raising the physicians' awareness regarding Young Carers in oncology : an interventional research. Pauline Justin, Géraldine Dorard, Aurélie Untas

O30 - Improving emotion regulation in breast cancer patients in the early survivorship period : Efficacy of a brief ecologically boosted group intervention. Pauline Waroquier, Isabelle Merckaert, Marie Caillier, Oriane Verkaeren, Sadio Righes, Aurore Liénard, Yves Libert, Darius Razavi

POSTER PRESENTATIONS

P1 - The role of senescence in the development of non- melanoma skin cancer in kidney transplant recipients : the impact of immunosuppressive drugs in vitro. Abi-Rached Henry; Bounaud Sophia; Martin Nathalie; Glowacki François, Mortier Laurent, Abbadie Corinne

P2 - Role of the microenvironment on the resistance of leukemia cells to tyrosine kinase inhibitors, contribution of bioprinting. Mélanie Dhayer, Nicolas Germain, Salim Dekiouk, Philippe Marchetti

P3 - O-GlcNAcylation of Thymidylate Synthase : a new regulatory mechanism of 5-Fluorouracil chemotherapy response in colorectal cancer. Ninon VERY, Stéphan HARDIVILLE, Tony LEFEBVRE, Ikram EL YAZIDI-BELKOURA

P4 - Development of a "metastasis-on-a-chip" to monitor cancer cells extravasation during metastatic process in breast cancer. Flavie WOESTELAND, Aude SIVERY, Marie DENOULET, Mathilde BRULE, Anaïs HOROCHOWSKA, Fabrice SONCIN, Xuefen LE BOURHIS, Anthony TREIZEBRE, Chann LAGADEC

P5 - Resistance of s-SHIP positive tumor cells in the MMTV- Wnt1 mouse model of breast cancer. Joséphine Louvieaux, Roland Bourette

P6 - Study of the role of MUC1 on the properties and phenomena of chemoresistance to cisplatin in lung cancer cells. Marine Goujon, Michaël Perrais, Jean Baptiste Gibier

P7 - Involvement of TrkA/CD44v3 signaling in metastasis formation in triple negative breast cancer. Alexandre Van Outryve; Julien Cicero; Sarah Trouvilliez; Martine Palma; Eloise Happernegg; Xuefen Le Bourhis ; Fabrizio Cleri; Robert-Alain Toillon

P8 - Role of androgens in SARS-CoV-2 viral infection and COVID-19 progression. Aline Hantute-Ghesquier, Anthony Turpin, Valentin Sencio, Anne Flourens, Nathalie Vanpouille, Cyril Robil, David Tulasne, Sandrine Belouzard, François Trottein, Martine Duterque-Coquillaud

P9 - Nasopharyngeal Carcinoma Exosomes Modulate the Properties of Human Dendritic Cells and Favour their Recruitment. Anthony Lefebvre, Camille Trioen, Sarah Renaud, William Laine, Benjamin Hennart, Delphine Allorge, Jerome Kluza, Elisabeth Werkmeister, Guillaume Grolez, Nadira Delhem, Olivier Moralès

P10 - Identification of a chemosensitizing miRNA by a functional screening and characterization of associated target genes : towards new therapeutic strategies for ovarian cancers. Celia Brochen, Mégane Vernon, Matthieu Meryet-Figuière, Bernard Lambert, Emilie Brotin, Nicolas Vigneron, Mohammad Ahmad, Jean-Paul Issartel, Edwige Abeilard, Florence Giffard, Laurent Poulain and Christophe Denoyelle

P11 - ABSP : A new automated R tool to analyze Bisulfite Sequencing PCR (BSP), to facilitate the study of target regions DNA methylation. Marie Denoulet, Mathilde Brulé, François Anquez, Audrey Vincent, Julie Schnipper, Eric Adriaenssens, Robert-Alain Toillon, Xuefen Le Bourhis and Chann Lagadec

P12 - Sodium – Calcium Signaling Undergoing Metastatic Potential of Prostate Cancer cells. Dheeraj KANNANCHERI PUTHOORU, Charlotte DUBOIS, Valerio FARFARIELLO, Francoise FARACE, Arnaud MONTEIL, Natalia PREVARSKAYA

P13 - IRE1 RNase controls CD95-mediated cell death. Diana Pelizzari-Raymundo, Matthieu Le Gallo, Raphael Pineau, Alexandra Papaioannou, Sophie Martin, Tony Avril, Eric Chevet, Elodie Lafont

P14 – SENSARCOME : Targeting radio-induced senescence to prevent secondary sarcomas in irradiated field. Elodie Rodzinski, Nathalie Martin, Clémentine De Schutter, Corinne Abbadie

P15 - Identification of Merkel cell polyomavirus' oncogenic interactions. Kamel Bachiri, Diala Kantar, Michel Salzet, Etienne Coyaud

P16 - TRPM4 regulates cytosolic Ca2+ oscillations and secretome in chemotherapy-induced senescence. Lina Mesilmany, Maya Yassine, Sylvie Radoslavova, Alessandra Fiorio Pla, Haidar Akl, Valerio Farfariello, Natacha Prevarskaya

P17 - The role of TNF-alpha in thymus dysfunction during AML. Meriem Ben Khoud, Nathalie Jouy, Nicolas Barois, Bruno Quesnel and Carine Brinster

P19 - The first peptide ligand targeting the EGF2 domain of MUC4 rescues Herceptin accessibility in pancreatic cancer cell in vitro. Nicolas Stoup, Maxime Liberelle, Nicolas Renault, Thomas Meynard, Patricia Melnyk, Nicolas Lebègue, Isabelle Van Seuningen

P20 - Istradefylline (KW6002) protects from cisplatin-induced nephrotoxicity while preserving cisplatin anti-tumor effects. Sandy Fellah, Edmone Dewaeles, Kevin Carvalho, Nihad Boukrout, Cynthia Van Der Hauwaert, Nathalie Martin, Jhenkruthi Vijayashankara, Viviane Gnemmi, Nicolas Pottier, Michaël Perrais, David Blum, Christelle Cauffiez

P21 - Mechanobiological characterization of a 3D in vitro pancreatic ductal adenocarcinoma model and the study of tumor-stroma interaction. Thomas Meynard; Félix Royer; Sonia Paget; Zied Souguir; Antonino Bongiovani; Audrey Vincent; Vincent Senez and Isabelle Van Seuningen

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