ARTP
Association pour la Recherche sur les Tumeurs de la Prostate

ARTP BULLETIN

November 19th, 2025

34th Annual Meeting Association pour la Recherche sur les Tumeurs de la Prostate

Foreword

The ARTP symposium stands at a leading forum that brings together international researchers, academics, and clinicians who are devoted to advancing the science and clinical management of prostate cancer. The meeting fosters rigorous exchange and the presentation of novel findings and encourages interdisciplinary collaboration, all of which drive progress in our field. The funding for the newly selected 2025 research projects and the organization of this conference were made possible by the generous support of Pierre Fabre Médicament, the Association Française d'Urologie, Astellas, AstraZeneca/MSD, Accord Healthcare, and Pfizer. We extend our sincere gratitude to these partners and thank all speakers and participants for their contributions and engagement.

Pr Arnauld VILLERS, ARTP President

AFU Association Française d'Urologie
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34th Annual Meeting
Wednesday 19 November 2025
Palais des Congrès de Paris
2 place de la Porte Maillot
75017 Paris

"Insights into Nuclear Receptors, Epigenetics, and Transcriptomics Landscapes of Prostate Cancer"

8:15 a.m. : Registration (3rd floor)

9:00 a.m. : **Welcome** Arnauld Villers, ARTP President

9:05 a.m : **Session I : ARTP Grant Laureates**
Chairs : Valério Farfariello, Catherine Muller

- **Marina PINSKAYA** (Institut Curie, CNRS UMR 3244, Paris)
  'Early activated long noncoding RNA as a potential modulator of cell plasticity in CRPC '
- **Eva ERDMANN** (IGBMC, Inserm U964, CNRS UMR 7104, Strasbourg)
  'Molecular Mechanisms of Deregulation of Cellular Plasticity in Prostate Cancer: Study of a Potential Protective Role of the Androgen Receptor'
- **Margaux HERMIEU** (Ecole Nationale Vétérinaire d'Alfort, Maisons-Alfort)
  'Contribution of canine olfaction in the diagnostic strategy of intermediate and high-risk prostate cancer; a double-blind validation study'

9:55 a.m. : Coffee Break & Visit of Exhibition Booths

10:15 a.m. : **SESSION II : Epigenetic and Transcriptomic Drivers of Prostate Cancer**
Chairs : Clémentine le Magnen, Damien Destouches

- **Carmen JERONIMO** (Portuguese Oncology Institute of Porto & University of Porto, Portugal)
  'The DNA Methylation Landscape of Prostate Cancer'
- **Wilbert ZWART** (The Netherlands Cancer Institute, Amsterdam, Netherlands)
  'Epigenetic regulation of AR action: from basic discovery to clinical trials and back again'
- **Sandy FIGIEL** (University of Oxford, UK)
  'Spatial Mapping of Clonal Heterogeneity and Stromal Dynamics in Prostate Cancer'

12:00 p.m. : Lunch

1:15 p.m. : **SESSION III : Clinical Session**
Chairs : Charles Dariane, Jonathan Olivier

- **Guillaume PLOUSSARD** (UROSUD, Toulouse)
  'Neoadjvant Treatments before Radical Prostatectomy with ARPI'
- **Michael BABOUDJIAN** (AP-HM, Marseille) & **Quang Hieu DUONG** (Inserm ERL 1326)
  'Patient-Derived Organoids as Tools for Personalized Prostate Cancer Therapy Using Smart Nanoparticles Targeting mRNA'
- **Cedric POBEL** (Institut Gustave Roussy, Villejuif)
  'Neuroendocrine tumors: Emergence of NE clones under hormonal deprivation'

2:20 p.m : Coffee Break & Visit of Exhibition Booths

2:45 p.m. : **SESSION IV : Nuclear Receptor Signaling in Prostate Cancer**
Chairs : Vincent Goffin, Laurent Morel

- **Ville PAAKINAHO** (University of Eastern Finland, Kuopo, Finland)
  'Transcription Factor Crosstalk Regulates Glucocorticoid Receptor Signaling in Prostate Cancer'
- **Andrea LUNARDI** (University of Trento, Italy)
  'Molecular Architects of the Prostate Luminal Lineage: at the Crossroads of Androgen and Retinoic Signaling'

3:45 p.m. : **SESSION V : Poster Session**
Chairs : Edith Bonnelye, Frédéric Bost
Les candidats au Prix du Meilleur Poster auront 3 minutes pour présenter leur poster
Candidates for the Best Poster Award will have 3 minutes to present their poster.

5:00 p.m. : **SESSION VI : 2024 ARTP Poster Prize Laureates**
Chairs : Edith Bonnelye, Frédéric Bost

- **Léa BOUHELIER** (IGBMC, Inserm U964, CNRS UMR 7104, Strasbourg)
  'NK Cells Play a Key Role in Castration Resistant Prostate Cancer'
- **Robin DOLGOS** (Dépt. de Biomédecine, Université de Bâle, Suisse)
  'ECM-free Patient-Derived Organoids Preserve Diverse Prostate Cancer lineAges and Uncover in Vitro-Enriched Cell Types'
- **Mathilde LACOMBE** (IPBS CNRS UMR 5089, Toulouse)
  'Bone Marrow Adipocyte-Derived Androgens: a Role in Progression and Castration Resistance of Bone Metastatic Prostate Cancer'

5:30 p.m. : **Assemblée Générale ARTP & Poster Prize Distribution**
Arnauld Villers, ARTP President
Olivier Cuvillier, ARTP Treasurer

5:45 p.m : End of the meeting

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Session I :
ARTP Grant Laureates

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Marina PINSKAYA

Institut Curie, CNRS UMR 3244, Paris

'Early activated long noncoding RNA as a potential modulator of cell plasticity in CRPC'

Androgen-deprivation therapy forces prostate tumors to adapt, promoting the emergence of castration-resistant and neuroendocrine states through lineage plasticity. We identified the long noncoding RNA - PROCA11 - as an early transcriptional responder to androgen deprivation that persists during neuroendocrine transdifferentiation. PROCA11 is highly expressed in advanced adenocarcinoma, CRPC and NEPC tumors. It modulates cell survival, proliferation, and migration by attenuating apoptosis and enhancing adhesion, potentially through interactions with the cell-cycle regulator CCAR2/DBC1 and the cell adhesion protein α-Catenin.

This work identifies PROCA11 as a potential modulator of both cell survival and identity, providing new insight into how long noncoding RNAs contribute to the adaptive transition toward therapy-resistant prostate cancer.

Session I :
ARTP Grant Laureates

1

Eva ERDMANN

IGBMC, Inserm U964, CNRS UMR 7104, Strasbourg

'Molecular Mechanisms of Deregulation of Cellular Plasticity in Prostate Cancer: Study of a Potential Protective Role of the Androgen Receptor'

Androgen receptor (AR), a member of the nuclear receptor superfamily, orchestrates critical pathways that support prostate cancer (PCa) growth and survival. Despite an initial therapeutic response, inhibition of AR pathway used in advanced PCa often leads to the development of castration-resistant prostate cancer (CRPC), recurrently characterized by the presence of ligand-independent AR splice variants (AR-Vs) such as AR-V7. Besides their role in tumor cell proliferation in the absence of androgens, AR-Vs can exacerbate cell aggressiveness by promoting genes involved in the epithelial-to-mesenchymal transition (EMT), a key process in cellular plasticity.

Our studies on the functional properties of these constitutively active AR-Vs have highlighted a lesser-known role of AR in prostate epithelial cells. Indeed, transcriptomic and proteomic approaches as well as functional enrichment analyses led us to establish that AR is normally involved in transcriptional repression of a panel of genes involved in cell plasticity, and that AR-Vs pathologically lose this specific repression capacity. Also, analysis of protein partners by the BioID approach suggested a lower recruitment of repressors by AR-Vs compared to AR.

To go deeper in the molecular mechanisms associated with this dual function of AR and AR-Vs on cell plasticity, we focus on the regulation of the human CDH2 gene encoding N-cadherin, a key EMT marker normally repressed by AR. Our previous work has demonstrated that AR-V7, unlike AR, can induce CDH2 expression. Data mining, protein-DNA interaction and gene expression analyses were performed in prostate cancer cells. We showed that this control of N-cadherin by AR and AR-V7 occurs through a human specific variable number tandem repeat (VNTR) located within the first intron of the human CDH2 gene that should be considered as a potential transcriptional hub for different transcription factors. Indeed, this regulatory region is also recognized by glucocorticoid receptor (GR), and GR activities from this VNTR are similar to AR-V7 ones.

Thus, prostate tumor cells may unlock an up to now unknown molecular mechanism associated with a fine-tuned control of human CDH2 gene expression.

Altogether, our observations support a model in which androgens and full-length AR signaling negatively regulate cell plasticity in prostate epithelial cells and that this repressive function could be pathologically abrogated by AR variants and GR in PCa.

Session I :
ARTP Grant Laureates

1

Margaux HERMIEU

Ecole Nationale Vétérinaire d'Alfort, Maisons-Alfort

'Contribution of canine olfaction in the diagnostic strategy of intermediate and high-risk prostate cancer; a double-blind validation study'

Purpose: Prostate cancer diagnosis is confirmed with a prostate biopsy, which is invasive and unpleasant. Adding canine olfaction into the diagnostic protocol could help avoid unnecessary biopsies. This study aims to determine whether dogs can identify ISUP (International Society of Urological Pathology) > 2 prostate cancer.

Materials and methods: This double-blind, prospective, validation study included men with suspected prostate cancer between November 2022 and April 2023 in France. They were classified into two groups according to their prostate biopsy results; cases (ISUP > 2) and controls (ISUP < 1 or negative). Seven dogs analyzed their urine. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for canine olfactory detection of ISUP ≥ 2 prostate cancer were measured and compared with that of prostate MRI versus prostate biopsy.

Results: The seven dogs analyzed 151 urine samples, 78 from the case group and 73 from the control group. The minimal and maximal observed values were 54% and 86% for sensitivity, and 69% and 88% for specificity. Five dogs had a sensitivity above 73% and six dogs had a specificity above 75%. The kappa coefficient quantifying agreement between the biopsy result and the MRI PI-RADS ≥ 3 was 0.17 [- 0.14; 0.17], 0.20 [0.02-0.33] for PI-RADS ≥ 4 and 0.64 [0.5-0.75] for canine olfaction meaning there is a substantial agreement between the biopsy result and canine olfaction.

Conclusions: Based on this study, the non-invasive and safe canine olfaction technique seems reliable for diagnosing ISUP ≥ 2 prostate cancer. Combined with prostate MRI, it may improve the decision-making process when choosing to perform prostate biopsies.

Session II : Epigenetic and Transcriptomic Drivers of Prostate Cancer

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Carmen JERONIMO

Portuguese Oncology Institute of Porto & University of Porto, Portugal

'The DNA Methylation Landscape of Prostate Cancer'

Session II : Epigenetic and Transcriptomic Drivers of Prostate Cancer

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Wilbert ZWART

The Netherlands Cancer Institute, Amsterdam, Netherlands

Epigenetic regulation of AR action: from basic discovery to clinical trials and back again'

Epigenetic gene regulation plays a pivotal role on AR action. We and others have observed extensive epigenetic plasticity in prostate cancer development and progression, the implications thereof remain only partly understood. Through implementing our functional genomics technologies in prospective clinical trials, we discover the basic rules and commonalities of epigenetic alterations, that may shape therapy response and resistance. These observations are tested for causality in preclinical models, and ultimately coupled back again to new trial design. Such a Full Circle cancer research design, greatly accelerates not only our basic mechanistic understanding of the disease, but at the same time enhances innovative steps in improving prostate cancer care.

Session II : Epigenetic and Transcriptomic Drivers of Prostate Cancer

2

Sandy FIGIEL

University of Oxford, UK

'Spatial mapping of clonal heterogeneity and stromal dynamics in prostate cancer'

Prostate cancer is the most common malignancy in men, yet its clinical behaviour remains highly unpredictable. While some tumours remain indolent, others progress aggressively and metastasise. Current prognostic markers are insufficient to reliably distinguish these outcomes, leading to both overtreatment and undertreatment.

Our research seeks to understand the molecular and structural determinants of prostate cancer aggressiveness by integrating spatial transcriptomics, spatial proteomics, and advanced 3D imaging. Spatial transcriptomics enables high-resolution mapping of tumour clonal architecture, tracing the evolutionary trajectories of aggressive clones and revealing their interactions with the surrounding microenvironment, including immune and stromal components. Spatial proteomics further characterises protein expression and cell-cell organisation, providing functional context to these molecular landscapes.

To complement these molecular approaches, we are developing a 3D imaging platform using open-top light-sheet microscopy (OTLS). This technology allows high-resolution visualisation of intact, cleared tissues, capturing the full architecture of tumours and their microenvironment. By resolving structural features and spatial relationships that are invisible in 2D sections, 3D imaging enhances our understanding of tumour evolution, vascularisation, and stromal interactions.

By combining multi-omic spatial mapping with 3D tissue architecture, we aim to identify the cellular and molecular features that drive tumour progression and metastasis. This integrated framework holds promise for improving prognostic accuracy and guiding precision therapies in prostate cancer.

Session III : Clinical Session

3

Guillaume PLOUSSARD

UROSUD, Toulouse

'Neoadjvant treatments before radical prostatectomy with ARPI'

Session III : Clinical Session

3

Michael BABOUDJIAN & Quang Hieu DUONG

AP-HM, Marseille and Inserm ERL 1326

'Patient-Derived Organoids as Tools for Personalized Prostate Cancer Therapy Using Smart Nanoparticles Targeting mRNA'

Patient-derived organoids (PDOs) have emerged as powerful preclinical models that closely preserve the cellular heterogeneity, histopathology, and molecular features of the original tumor. In prostate cancer (PC), therapeutic development is often hindered by a lack of physiologically relevant models that faithfully recapitulate disease complexity. PDOs are an ideal model for studying castration-resistant prostate cancer progression (CRPC) and identifying patient groups with common molecular abnormalities for targeted therapies. However, their application in organoid-based systems remains underexplored. Antisense oligonucleotides (ASOs) are an emerging class of precision medicines, offering high target specificity and the ability to modulate gene expression at the RNA level. To improve the stability, bioavailability, and delivery of ASOs, our laboratory developed a third generation of ASOs using lipid-conjugated oligonucleotides (LASOs). Our work demonstrated that lipids enabled cellular internalization of ASOs without a transfection agent via macropinocytosis. We interestingly demonstrated that the amphiphilic LASOs can spontaneously self-assemble into nanoparticles (NP), forming a hydrophobic core to encapsulate chemical compounds and serve as nanocarriers to deliver cytotoxic chemotherapy. Since PDOs represent a reliable model for developing a new class of "smart' nanomedicine based on the LASO technology for personalized treatments for CRPC, we established a biobank of PC-derived PDOs with a high initial growth success rate (>95%) and confirmed that they retain key histological and molecular markers, including CK5, CK8, PSMA, AR, AMACR, and HSP27, a promising ASO-targeted for CRPC treatment. Our PDO model paves the way for personalized treatments, combining ASO-based therapies, nanomedicine, and conventional treatments (castration) to achieve a synergistic effect and improved therapeutic efficacy.

Session III : Clinical Session

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Cédric POBEL

Institut Gustave Roussy, Villejuif

‘Neuroendocrine tumors: Emergence of NE clones under hormonal deprivation’

Session IV : Nuclear Receptor Signaling in Prostate Cancer

4

Ville PAAKINAHO

University of Eastern Finland, Kuopo, Finland

'Transcription factor crosstalk regulates glucocorticoid receptor signaling in prostate cancer'

The glucocorticoid receptor (GR) exhibits context-dependent roles in prostate cancer. In therapy-naïve settings, GR can exert tumor-suppressive effects, whereas in antiandrogen-treated disease, GR hijacks the oncogenic role of the androgen receptor (AR), replacing the inactivated AR and driving antiandrogen resistance. Despite this functional switch, the mechanisms underlying GR's divergent actions across disease stages remain poorly understood. This distinction is clinically relevant, as prostate cancer patients frequently receive glucocorticoids to manage inflammation and therapy-related side effects. Given that transcription factor (TF) crosstalk influences cancer progression and drug resistance, and GR's interactions with other TFs are highly context-dependent, such crosstalk may explain GR's dual roles. To investigate this, we integrated genome- and proteome-wide data and identified key features of GR action in prostate cancer cells. We found that GR replaces AR at pre-accessible chromatin sites marked by FOXA1 occupancy in antiandrogen-exposed cells. Chromatin proteomics further revealed a markedly expanded GR interactome under antiandrogen conditions. Additionally, GR's chromatin binding and transcriptional activity varied across prostate cancer subtypes and immortalized prostate cell lines. Together, our findings provide mechanistic insight into how GR functions in antiandrogen-exposed prostate cancer cells, and how its role transitions from tumor suppressive to oncogenic depending on TF crosstalk.

Session IV : Nuclear Receptor Signaling in Prostate Cancer

4

Andrea LUNARDI

University of Trento, Italy

'Molecular architects of the prostate luminal lineage: at the crossroads of androgen and retinoic signaling'

Retinoic acid (RA) signaling plays crucial roles in tissue differentiation, including in the reproductive system. Exploiting prostate organoid technology, we demonstrate that RA-dependent RARγ activation triggers Foxa1 expression, which synergizes with the androgen pathway for luminal compartment expansion, cytoarchitecture and function. Combining functional genetics with ChIP-seq analyses and structural modeling, we characterize FOXA1F254E255 as a loss-of-function mutation with impaired transcriptional function and luminal fate commitment of prostate progenitors. Overall, we define RA-FOXA1 as an instructive signal for glandular identity with important implications in prostate tumorigenesis.

Session V : Poster session

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STUDY OF THE MECHANISMS OF OCCURRENCE AND EVOLUTION OF EARLY EPITHELIAL TUMOR. IMPLICATIONS FOR PROSTATE CARCINOGENESIS

Elissa Baabdaty, Marine Vialat, Amalia Trousson, Françoise Degoul, Jean-Marc A. Lobaccaro, Silvère Baron, Laurent Morel & Cyrille de Joussineau

iGReD – France

The Notch signaling pathway is evolutionarily conserved and plays a crucial physiological role in cell fate determination and tissue homeostasis, but also a pathological role in carcinogenesis. However, its implication in prostate tumorigenesis remains ambiguous, with contradictory observations regarding its promoting or inhibitory effect on tumor growth and evolution, without a comprehensive understanding of the underlying mechanisms. Our team has previously developed a model of prostate tumorigenesis in vivo, using a structural and functional equivalent of a prostatic acinus, the accessory gland of Drosophila melanogaster. This model is based on clonal expression of the oncogene EGFRλ which allows precise quantification of tumor formation following basal extrusion phenomenon, and the characterization of tumor cell progression based on their localization, number and expression of markers of aggressiveness. In this context, we have deciphered the influence of the different components of the Notch pathway on tumor initiation, progression and resistance. Remarkably, our results reveal the existence of two antagonistic signaling within the Notch pathway. On the one hand, canonical Notch-dependent signaling displays an anti-tumoral action. On the other hand, depending of Notch ligand Delta, a predominant and separated signaling occurs, which itself strongly promotes tumorigenesis. These findings rationalize previous contradictory observations and suggest targeted therapeutic avenues to achieve specific anti-tumor effects.

Session V : Poster session

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STAT5 IS ACTIVATED IN BENIGN PROSTATIC HYPERPLASIA IN MEN

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Background

The only etiologic treatment for benign prostatic hyperplasia (BPH) is the 5-alpha-reductase inhibitor (5ARI). However, its limited efficacy and side effects justify the search for new therapeutic targets. STAT5 is a transcription factor that promotes proliferative and anti-apoptotic effects on the prostate epithelium of rodents. Its activation in the prostate of transgenic "Pb-PRL" mice induces a BPH phenotype.

The main objective of this work was to determine if STAT5 is activated in human BPH and to identify the mechanisms involved in order to explore new therapeutic targets.

Methods

103 consecutive patients operated on for symptomatic BPH were included. Fresh tissue was collected in the operating room for primary organoid culture. The rest of the resected tissue was fixed and embedded in paraffin for immunohistochemical analysis. 8 prostates from deceased organ donors without prostatic disease were included to form a control cohort and treated according to the same protocol. STAT5 activators (ligands/receptors) were studied by bioinformatics analysis of human prostate single-cell RNA sequencing database.

Results

Quantitative analysis of STAT5 activation (nuclear staining) revealed a significant increase in patients operated on for BPH compared to the control cohort (15% vs 1.4%; p=0.0009). The majority of cells showing STAT5 activation were located in the luminal position of the epithelial compartment, mimicking the staining observed in Pb-PRL mice. Nuclear staining of STAT5 was also observed in some stromal and inflammatory cells. This staining was significantly increased in patients treated with 5ARI compared to untreated patients (36% vs 22%; p=0.0193).

Bioinformatics analysis revealed an increase in transcripts of the Leukemia Inhibitory Factor receptor (LIF-R) in luminal cells of patients. LIF activates STAT5 in the human prostate cell line RWPE-1 and induces a proliferative effect on human prostate organoids.

Conclusions

Due to its well-documented trophic capabilities, the STAT5 pathway, potentially activated by LIF, could play a key role in the pathophysiology of human BPH. Further studies should explore STAT pathway as a therapeutic target.

Session V : Poster session

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ORAI3 UN NOUVEAU MÉDIATEUR DE LA COMMUNICATION NERF-TUMEUR ET DE LA PLASTICITÉ CELLULAIRE DU CANCER DE LA PROSTATE

Lucie BOURGUEDIEU[1], Clément VANDRISSE[2], Fabien VANDEN ABEELE[1], Charlotte DUBOIS[2]

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Contexte :

La progression et la résistance thérapeutique du cancer de la prostate (CPa) sont intrinsèquement liées à deux phénomènes majeurs : la plasticité tumorale et l'innervation accrue du microenvironnement. Notre recherche se focalise sur le canal calcique ORAI3, une protéine surexprimée dans les cellules épithéliales prostatiques tumorales qui pourrait constituer un point de convergence entre ces deux mécanismes.

Méthodes :

Nous avons déployé une approche méthodologique complète , combinant l'imagerie MALDI, des analyses Omics (sur culots cellulaires et coupes de tissus de CPa), des tests fonctionnels *in vitro* (imagerie calcique, migration, prolifération) et des études de signalisation (Western blot, angio array). Nous avons notamment utilisé la lignée cancéreuse agressive et androgéno-indépendante PC3, en développant un modèle de sur-expression stable d'ORAI3 ($PC3^{OE\text{-}ORAI3}$), ainsi que des co-cultures avec des cellules endothéliales (HUVEC) et neuronales (issues de ganglions rachidiens (DRG) de souris).

Résultats :

Nos résultats indiquent que la surexpression d'ORAI3 participent *in vitro* et *in vivo* au remodellage du microenvironnement tumoral (induction de la transition épithélio mésenchymateuse (TEM), et angiogenèse). Nous montrons également *in vitro* que les nerfs peuvent activer le canal ORAI3 et stimuler la TEM. Des résultats préliminaires de co-cultures et de milieux conditionnés obtenus à partir des cellules $PC3^{WT}$ ou $PC3^{OE\text{-}ORAI3}$, suggèrent que les cellules $PC3^{OE\text{-}ORAI3}$ peuvent stimuler la neuritogenèse et angiogenèse.

Conclusions :

Ces résultats identifient ORAI3 comme un médiateur de la communication bidirectionnelle nerf-tumeur et de la plasticité cellulaire du CPa. Nous avons développé un modèle murin développant un cancer spontané de la prostate, invalidé (inductible via système Cre-ERT2) pour Orai3. Ce modèle va nous permettre d' étudier le remodelage du microenvironnement tumoral induit par la perte d'Orai3 et/ou par les nerfs tumoraux. Cette stratégie devrait confirmer l'implication cruciale d'ORAI3 dans la carcinogenèse prostatique et révéler de nouvelles cibles pour prévenir les formes métastatiques actuellement incurables.

TO STUDY THE IMPACT OF PGC-1α ON LIPID METABOLISM IN PROSTATE CANCER

Suraj Narayanan CHEMBUKAVU[1], Michel KAHI[1], Constance NAU[1, 2], Abigail MAZZU[1], Joseph MURDACA[1], Pierre BERTRAND[2, 3], Pauline PERNE[2], Delphine DEBAYLE[2], Paraskevi KOUSTERIDO[2, 3], Fabienne GUILLAUMOND-MARCHAI[4], Johan SWINNEN[5], Pascal PERALDI[1], Nathalie MAZURE[1], Frédéric BOST[1]

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This project is a part of the MSCA Doctoral Network PROSTAMET – Grand Agreement No. 101120283, EU Horizon 2020

Background:

PGC-1α (Peroxisome proliferator-activated receptor gamma coactivator 1-alpha) is a transcriptional coactivator protein that has been known to play a critical role towards mitochondrial biosynthesis and lipid metabolism. Prior data from our lab has proven the regulatory mechanisms of PGC-1α towards the aggressiveness of prostate cancer, and the poor prognosis of patients presenting low levels of PGC-1α. The present study delves into the axis of PGC-1α, lipid metabolism, and prostate cancer aggressiveness.

Methods:

We explored the impact of overexpression of PGC-1α on the cellular energetics, metabolic switch, and fatty acid oxidation through functional analysis of mitochondrial metabolism. We further performed LC/MS lipidomic analysis in these cells to determine the impact of PGC-1α levels on the various lipid profiles in these cells. The specific findings from these experiments were further validated by performing pathway specific gene expression experiments to ascertain the specific role of PGC-1α on these pathways

Results:

We found that cells overexpressing PGC-1α showed significantly higher respiration than wild-type cells, and that PGC-1α overexpression restored respiration in metformin-treated cells to baseline levels.

Lipidomic analysis revealed that PGC-1α affects lipid saturation, with overexpressing cells showing reduced levels of unsaturated lipids. Additionally, lipids linked to the arachidonic acid pathway were elevated, and qPCR analysis supported PGC-1α's impact on both this pathway and peroxisomal fatty acid oxidation. Another observation of interest was the significant upregulation of triglycerides upon overexpression of PGC-1α, which has a wide range of metabolic consequences.

Conclusions:

PGC-1α is responsible for the elevation in respiration in prostate cancer cells and recovers respiration in cells treated with metformin. Furthermore, there is an elevated levels of triglycerides and unsaturated fatty acids upon overexpression of PGC-1α. There is a demonstrable alteration in the arachidonic acid pathway as well as peroxisomal metabolism of fatty acids.

Collectively, we see the possibility of a novel pathway linking PGC-1α, lipid metabolism and prostate cancer.

Session V : Poster session

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THE PRO-TUMORAL FUNCTIONS OF THE EPIGENETIC ENZYME SUV4-20H2 IN PROSTATE CANCER

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Despite significant progress in prostate cancer detection and treatment, this disease remains a major cause of cancer-related mortality. While localized disease can often be managed successfully, metastatic and therapy-resistant stages remain largely incurable, even after intensive multimodal regimens. Thus, understanding the molecular mechanisms driving tumor progression and therapeutic resistance is critical to develop more effective strategies. In this regard, we identified the lysine methyltransferase **SUV4-20H2**–responsible for catalyzing the trimethylation of histone H4 at lysine 20 (H4K20me3)–as a **key driver of prostate cancer growth and resistance**. Using xenografted mouse models, we demonstrate that genetic loss of SUV4-20H2 markedly impairs prostate tumor growth, in contrast to its paralog SUV4-20H1 also involved in H4K20 methylation. To investigate the underlying mechanisms, we performed transcriptomic profiling (*in-vitro* and *in-vivo* RNA-Seq) of SUV4-20H2-deficient tumors. These analyses revealed that SUV4-20H2 controls the expression of several gene networks linked to cancer progression, including m**etabolism, Wnt signaling, and inflammatory pathways**. Notably, its loss preferentially reduced the expression of genes involved in Glutamine metabolism while having limited impact on glycolytic programs. Consistent with this, functional assays revealed that SUV4-20H2-deficient prostate cancer cells are particularly sensitive to **Glutamine deprivation** than to Glucose withdrawal, highlighting a metabolic shift in the source of energy sustaining tumor growth upon loss of SUV4-20H2. Importantly, the transcriptional role of SUV4-20H2 seems uncoupled from its enzymatic activity**.** Altogether, these results establish SUV4-20H2 as a central regulator of prostate cancer progression through a newly identified non-catalytic transcriptional role in orchestrating the balance between **Glucose and Glutamine metabolism** in tumor cells. By linking epigenetic regulation to metabolic plasticity, SUV4-20H2 might represent a previously unrecognized vulnerability in prostate cancer biology.

Session V : Poster session

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INVESTIGATING THE ROLE OF THE HDL SCAVENGER RECEPTOR CLASS B TYPE 1 (SCARB1) IN ADVANCED PROSTATE CANCER

De Sousa M.[1,2,3], Boutourlinsky K.[1,2], Gonthier C[1,2]., De Joussineau C.[1,2], Baabdaty E.[1,2], De Haze A.[1,2], Sanchez P.[1,2], Lobaccaro J.M.[1,2,3] & Baron S.[1,2,3]

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[3]MSCA PROSTAMET - European Union's Horizon 2020 grant agreement No. 101120283.

Studies show cholesterol playing a key role in prostate cancer (PC) progression to metastases. Increased accumulation is observed in carcinomas and secondary sites, and it may help the passage from androgen-sensitive PC to castration resistant PC. More specifically, high density lipoproteins (HDL), responsible for the reverse transport of cholesterol facilitated by the SCARB1 receptor, influence growth and proliferation of cells. The overexpression of SCARB1 has been associated with the proliferative phenotype of different human prostate cell lines and is found in human clinical data in carcinomas and metastatic tissue compared to normal prostate tissue. This overexpression is also associated with lower levels of important oncosuppressors such as PTEN, TP53 and SMAD4, recognized as key players in the process of prostate cancerogenesis. Notably, the loss of SCARB1 greatly diminishes the ability of PC cells to proliferate and metastasize in mice, highlighting SCARB1 as a possible key player in cancer progression.

To examine metastatic progression tied to loss of PTEN, SMAD4, Tp53, we are developing a novel orthotopic mouse model using CRISPR-Cas9 and CRE-LoxP methods in Mouse Prostate Epithelial Cells (MPEC). In parallel, we are studying the invasive and proliferative effects of SCARB1 knockout in PC3 cells through cell culture assays (including tumoroid formation) and metastatic follow-up experiments *in vivo*. Additionally, we are investigating the role of SCARB1 orthologs in Drosophila Melanogaster's accessory gland (ortholog of the human prostate) using an existing model that exhibits tumorigenic phenotypes.

Altogether, this study will elucidate the precise role of SCARB1 and HDL-mediated cholesterol transport in the metastatic processes driving the progression of prostate cancer toward advanced disease.

Session V : Poster session

5

ANDROGEN RECEPTOR-RNAs INTERACTOME IN CELL PLASTICITY AND ONSET OF CASTRATION-RESISTANT PROSTATE CANCER

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BACKGROUND

Androgen receptor (AR) is a key player in prostate cancer development and progression, and its inhibition through androgen deprivation therapy (ADT) constitutes the first line of treatment. However, ADT often leads to the emergence of the more aggressive castration-resistant prostate cancer (CRPC) and its neuroendocrine-like form (NEPC), allowing androgen-independent tumor progression. This is achieved through several transient states with elevated heterogeneity and cellular plasticity, potentially still relying on AR signaling. Several TFs have been reported to bind RNA, which can modulate their function, even in the absence of a canonical RNA-binding domain. Moreover, several long noncoding lncRNAs as SLNCR in melanoma, and HOTAIR in prostate cancer, have been proven to bind AR. We aim to investigate the AR-RNAs interactome in response to ADT to assess its role in AR regulation in the context of prostate cancer progression towards androgen resistance.

METHODS

To assess AR-RNA direct interaction at the single-nucleotide level, we exploited iCLIP2 in the AR-dependent LNCaP cell line in presence or absence of androgen. The interactions will be visualized at single-molecule resolution through rISH-PLA. Finally, the function of the interaction will be assessed at the molecular level by CUT&RUN and RNA-seq. Parallelly, isoform-specific studies will be conducted using PacBio long-read sequencing.

RESULTS

LNCaP cell line androgen deprivation was carried out for >6 months; samples are currently undergoing PacBio sequencing and informative genes linked to progression were assessed at different timepoints through RT-qPCR. The iCLIP2 protocol was optimized, and libraries are now being prepared for several timepoints.

CONCLUSIONS

Further work is needed to optimize iCLIP2 libraries and to extract RNA interactions during resistance to ADT. Moreover, long-read sequencing will provide further information on prostate cancer progression at the isoform level. Additionally, APEX-seq will validate or challenge iCLIP2 results, coupling RNA with mass spectrometry data, which will allow further understanding of the AR regulatory network.

LE MICRO-ENVIRONNEMENT TUMORAL PROSTATIQUE EN REPONSE A LA RADIOTHERAPIE FLASH

Mots clés : Radiothérapie FLASH, fibrose, cancer prostatique, péricytes, remodelage vasculaire

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Le cancer prostatique demeure une cause majeure de mortalité et la radiothérapie est l'un des piliers de son traitement. Toutefois, les effets secondaires limitent les doses administrables. Dans ce cadre, la radiothérapie à ultra-haut débit de dose (RT-UHDD), dite "FLASH", permettrait de mieux préserver les tissus sains tout en conservant théoriquement l'efficacité antitumorale [1]. Or, les effets anti-tumoraux restent pourtant trop peu documentés.

Notre étude visait à comparer les effets de la RT-UHDD et de la radiothérapie conventionnelle (RT-CONV) sur le microenvironnement tumoral prostatique [2]. En particulier, le remodelage vasculaire, le recrutement péricytaire, la fibrose et leur lien potentiel avec la réponse immunitaire ont été recherchés dans un modèle murin d'adénocarcinome prostatique (PC3).

Nos résultats montrent que la RT-CONV et la RT-UHDD provoquent un recrutement accru de péricytes. Cependant, la RT-CONV semble favoriser le type 1 (α-SMA+, PD-L1+) tandis que la RT-UHDD induit préférentiellement des péricytes de type 2 (desmine+). De plus, l'expression tumorale globale de PD-L1 était plus faible après RT-UHDD qu'après RT-CONV. Enfin, la RT-CONV induit une fibrose également plus marquée.

Ces résultats suggèrent que la RT-UHDD modifie le microenvironnement tumoral de manière plus favorable à une réponse immunitaire antitumorale. Cela ouvre la voie à des stratégies combinées, notamment avec des thérapies immunomodulatrices. Des études supplémentaires seront nécessaires pour confirmer ces observations et valider leur pertinence clinique.

[1] Favaudon *et al.*, Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice. Sci Trans Med 2014.

[2] Potiron *et al.*, Improved functionality of the vasculature during conventionally fractionated radiation therapy of prostate cancer. PloS One 2013.

Session V : Poster session

5

THE K-RAS PUZZLE: UNLOCKING THE SECRETS OF K-RAS OLIGOMERIZATION TO TARGET PROSTATE CANCER

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This project is a part of the MSCA Doctoral Network PROSTAMET - Grand Agreement No. 101120283, EU Horizon 2020.

Background:

K-RAS (Kirsten-Rat Sarcoma viral oncogene) protein, known as the beating heart of signal transduction, is a membrane GTPase that acts as a molecular switch to control pathways involved in cell survival and proliferation. In Prostate Cancer (PCa), K-RAS mutations that stabilize K-RAS in its active state, promote tumour stemness, metastatic progression and bone metastasis. Plasma membrane-associated K-RAS forms dimers and nanoclusters that serve as effectors' recruitment and activation sites. However, evidence for K-RAS oligomerization in solution remains inconclusive. Studies indicate that K-RAS dimerization appears to rely on weak, transient protein-protein interactions (PPIs), leading to dimers that are difficult to detect without the concentrating effect of a lipid membrane. To date, only Muratcioglu et al. (1) and Tran et al. (2) have successfully spotted K-RAS oligomers in solution so far. Understanding K-RAS oligomerization dynamics in solution may reveal new opportunities for therapeutically targeting oncogenic RAS signalling in PCa.

Methods:

Recombinant human K-RAS was overexpressed in E. coli and purified by Immobilized Affinity Chromatography and Size Exclusion Chromatography (SEC). K-RAS oligomerization was detected in solution by Isothermal Titration Calorimetry, SEC, SEC Multi-Angle Light Scattering and Dynamic Light Scattering.

Results:

Here, we show that K-RAS was able to oligomerize intrinsically in solution, without the addition of any substrate that induce its oligomerization, possibly due to endogenous GDP. We were also able to obtain the dimer of Tran et al. by using a synthetic inducer, both experimentally and in silico.

Conclusions:

Our findings suggest that transient PPIs between K-RAS molecules can promote dimerization in solution, even in the absence of lipid membrane or activating substrates. This process seems concentration-dependent. The mediation of lipids might be essential for K-RAS nanoclustering, but not for dimerization. Our goal is to target these soluble dimers and develop novel therapeutics against the challenging-to-drug K-RAS in PCa.

(1) Muratcioglu et al., Structure 23 (2015)
(2) Tran et al., PNAS 117 (2020)

Session V : Poster session

5

REDUCED STORE-OPERATED CALCIUM ENTRY CONTRIBUTES TO AUTOPHAGY MEDIATED ESCAPE OF PROSTATE CANCER TO OXALIPLATIN TREATMENT

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Background:

Oxaliplatin, a third-generation platinum-based chemotherapeutic agent, exerts its anticancer effects primarily by inducing cell cycle arrest and apoptosis in prostate cancer cells. However, its therapeutic efficacy is often compromised by both intrinsic and acquired resistance mechanisms. Increasing evidence indicates that chemotherapeutic agents can activate autophagy, a cellular recycling and survival mechanism that contributes to the development of drug resistance. Calcium (Ca^{2+}) signaling is a critical regulator of cellular homeostasis and fate determination. Nevertheless, the specific roles of Ca^{2+} dynamics and Ca^{2+} channels in mediating oxaliplatin resistance in prostate cancer cells remain poorly defined and are subject to ongoing debate.

Methods:

Calcium Imaging, Immunoblotting, q-PCR, Cell-death Assays, Confocal Imaging, etc

Results:

In this study, we demonstrate that oxaliplatin treatment induces autophagic activity in prostate cancer cells. Concurrently, oxaliplatin modulates the expression profile of key components of the store-operated calcium entry (SOCE) pathway, characterized by upregulation of Orai3 channels and downregulation of Orai1 and Stim1. These molecular alterations lead to a reduction in SOCE activity, thereby contributing to the development of an apoptosis-resistant phenotype. Notably, silencing Orai3 expression in combination with autophagy inhibition restores oxaliplatin sensitivity and promotes apoptosis in prostate cancer cells. Collectively, our findings indicate that concurrent targeting of Orai3 and autophagy may potentiate the therapeutic efficacy of oxaliplatin and provide a promising strategy to overcome chemoresistance in prostate cancer.

Conclusion:

These findings shed light on the intricate interplay between calcium signaling, autophagy, and therapeutic resistance in PCa against oxaliplatin treatment, suggesting that selective targeting of specific Ca^{2+} channels could represent a promising approach to enhance treatment efficacy and prevent disease relapse.

STRUCTURAL AND BIOPHYSICAL INSIGHTS INTO ACSS2 FUNCTION: LINKING ENZYME ACTIVITY TO LIPID METABOLISM IN PROSTATE CANCER

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Background

Acetyl-CoA Synthetase 2 (ACSS2) catalyzes the conversion of acetate into acetyl-CoA, a key substrate for lipid metabolism and histone acetylation. It is overexpressed in prostate cancer, supporting tumor survival and growth under metabolic stress. However, the regulation and structural elucidation of ACSS2 remain poorly understood. Solving the structure of ACSS2 and screening repurposed drug libraries could reveal new therapeutic strategies targeting cancer metabolism.

Methods

Recombinant human ACSS2 protein is overexpressed and purified from E. coli cells. Mass photometry, SPR, and SAXS analysis are used to confirm the oligomeric state of the protein in solution. For structural characterization, cryo-EM screening of ACSS2 is initiated under near-native conditions. Alongside structural studies, a biochemical assay for drug screening was conducted to identify novel inhibitors for use in PCa cell lines. Tracer lipidomics will then be performed on these cell lines to monitor intracellular acetate, lipid distribution, and drug efficacy for pharmacological evaluation.

Results

Mass photometry revealed monomeric, dimeric, and trimeric forms of ACSS2, suggesting transient self-interaction. SPR confirmed a low affinity of the ACSS2 protein-protein interaction with a KD of approximately 10 µM. SAXS analysis indicated the possible formation of short filamentous chains at high protein concentrations, consistent with preliminary cryo-EM observations. Cryo-EM analysis achieved a high resolution of approximately 3 Å for the monomeric ACSS2 species, which is currently under analysis. Initial drug screening identified two novel inhibitors that bind to ACSS2. Further drug screening will identify additional candidates to be tested in tracer lipidomics experiments on PCa cell lines.

Conclusions

These findings suggest that ACSS2 can transiently self-associate, a feature that may regulate its catalytic activity under metabolic stress. Integrating structural and lipidomic data offers new insights into how ACSS2 supports lipid metabolism in prostate cancer, highlighting it as a promising target for metabolic intervention.

EPIGENETIC DEREGULATION CONTRIBUTES TO METABOLIC REPROGRAMMING AND THERAPY RESISTANCE IN PROSTATE CANCER

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Introduction:

Epigenetic deregulation contributes to metabolic reprogramming and therapy resistance in prostate cancer (PCa). This study investigated how DNA methylation and histone acetylation coordinate lipid metabolic regulation during PCa progression.

Materials and Methods:

We performed integrative multi-omics analyses combining DNA methylation, gene expression, chromatin accessibility, and histone acetylation data from 24 primary tumor samples. Validation was conducted in TCGA and GDC PRAD cohorts (n = 1140). Motif enrichment (HOMER) and transcription factor prediction (LISA) analyses were used to identify upstream regulators.

Results:

We identified 57 promoter-hypermethylated and downregulated genes enriched in lipid metabolism and oxidative stress regulation. To focus on purely epigenetic events, genes with copy-number variations were excluded. The selected genes showed the strongest negative correlation between promoter methylation and expression, indicating methylation-driven silencing. Chromatin accessibility correlated positively with expression for 44 of 57 genes, confirming epigenetic suppression as a major mechanism. Motif analysis revealed AR, RXRG/RARG, CEBPB, and KLF14 as key regulators linking these changes to lipid and mitochondrial pathways. An independent cohort of 86 normal prostate epithelium, 32 primary tumors, and 17 mCRPC samples was analyzed to assess H3K27ac dynamics. This analysis identified 243 lipid metabolism-related genes with mCRPC-enriched H3K27ac promoter sites, showing activation of anabolic lipid genes such as SCARB1, FASN, ELOVL6, and DGAT1 that promote metabolic adaptation and tumor aggressiveness.

Conclusions:

DNA methylation represses lipid oxidation pathways, while histone acetylation activates lipogenic programs, enforcing a glycolytic/lipogenic metabolic shift that promotes tumor aggressiveness and resistance. Future work will focus on targeted epigenetic reversion and functional rescue experiments in prostate cancer cell models.

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NOVEL PATIENT-DERIVED ORGANOID XENOGRAFT MODELS REVEAL MOLECULAR AND CLINICAL TRAJECTORIES OF PROSTATE CANCER PROGRESSION

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Introduction

Patient-derived organoids (PDOs) are promising models for prostate cancer (PCa), but studies comparing organoids and patient outcomes remain scarce. Importantly, it is still unknown whether PDOs recapitulate treatment responses and disease evolution.

Here, we established advanced in vivo and in vitro models from two distinct PCa cases—a metastatic hormone-sensitive PCa (mHSPC) with AR wild type and P53/PTEN loss, and a castration-resistant PCa (CRPC) carrying the AR L702H mutation—and retrospectively evaluated their ability to mirror the patients' clinical trajectories.

Methods

PDOs were engrafted into NSG mice to generate xenografts (PDOXs), from which organoids (PDOXOs) were serially propagated. Model fidelity was assessed by immunohistochemistry, immunofluorescence, and whole-exome sequencing. PDOXOs were treated with a targeted drug panel reflecting each patient's clinical regimen and viability outcomes were assessed with CellTiter-Glo 3D. Secreted PSA was measured by ELISA. Multiplexed single-cell transcriptomics (MULTI-seq) was employed to evaluate the concordance between PDOX and PDOX models across generations, and to track lineage dynamics during longitudinal treatment of the PDOs.

Results

The two PDO models were successfully established as serially transplantable PDOX systems. Both retained patient-specific genomic alterations and displayed minimal transcriptomic drift between their *in vivo* and *in vitro* counterparts. The mHSPC model showed marked sensitivity to androgen deprivation (AD) and AR pathway inhibitors, while the CRPC model displayed glucocorticoid-mediated AR activation. Chemotherapeutics showed efficacy in both models, while the CRPC model only remained resistant to AR pathway inhibition, consistent with the patients' clinical response. Longitudinal scRNA-seq analysis of the mHSPC PDOs under AD revealed the emergence of a $PROX1^{+}/ALDH1A1^{+}$ subpopulation, also detected in patient recurrences, suggesting a potential link to aggressive relapse.

Conclusions

Newly-established PDOXs and derived PDOs closely mimic patient tumors both phenotypically and functionally, providing unique models to study drug response and treatment resistance in advanced PCa.

DEVELOPMENT OF PATIENT-DERIVED PROSTATE CANCER ORGANOIDS FOR ANTISENSE OLIGONUCLEOTIDE-BASED PERSONALIZED THERAPY

Key words: Prostate cancer (PC), Patient-derived organoids (PDOs), Antisense oligonucleotides (ASOs), mRNA targeting, Heat shock protein 27 (HSP27), Apartosen (OGX-427), precision medicine

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Background:

Patient-derived organoids (PDOs) have emerged as powerful preclinical models that closely preserve the cellular heterogeneity, histopathology, and molecular features of original tumors. In prostate cancer, the development of PDOs has been limited by low success rates and the overgrowth of benign cells. Antisense oligonucleotides (ASOs) are an emerging class of precision medicines, offering high target specificity and the ability to modulate gene expression at the RNA level. However, their application in organoid-based systems remains underexplored. While ASO effectively suppressed mRNA expression and inhibited cell growth in 2D cultures, its efficacy was markedly limited in 3D organoids, likely due to extracellular matrix and structural barriers. This study, thus aimed to establish a biobank of patient-derived prostate cancer (PC) organoids and optimize protocol for ASOs treatment in organoids-based systems.

Methods:

Patient-derived organoids (PDOs) were established from transurethral resection (TURP) and biopsy specimens obtained from patients diagnosed with castration sensive prostate cancer (CSPC), castration resistance prostate cancer (CRPC) and benign prostatic hyperplasia (BPH). Histological and molecular characterization revealed that key markers, including CK5, CK8, AR, PSMA, AMACR, STEAP1, EGF, PTEN, PSA, and HSP27, were consistently preserved in PDOs relative to their corresponding primary tissues. PDOs which high expression of HSP27 was selected for OGX-427, an ASO targeting HSP27 transfection.

Results:

Our research obteined 27 samples of organoids with a high initial growth success rate (>95%). Our PDOs remain the histological and molecular marker of original tissues. While OGX-427 effectively suppressed HSP27 expression and inhibited cell growth in 2D cultures, its efficacy was markedly limited in 3D organoids, likely due to extracellular matrix and structural barriers. By removing Matrigel and applying single-cell transfection, we achieved efficient ASO uptake and observed robust, dose-dependent inhibition of organoid growth.

Conclusions:

These findings underscore the utility of PDOs for evaluating ASO-based therapies and highlight their potential to accelerate the development of precision oncology strategies for PC and other malignancies.

Session V : Poster session

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LOSS OF LXR ENHANCES TUMOR GROWTH AND LEADS TO DENDRITIC CELL ACCUMULATION IN PRECLINICAL PROSTATE CANCER MODELS

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Background

Immunotherapies have shown limited efficacy in Prostate Cancer (PCa), in which immunologically "cold" microenvironment is mainly composed of suppressive and dysfunctional immune cells. Previous results from our laboratory showed that LXR double knock-out (LXR DKO) induces an accumulation of non-functional myeloid cells and promotes neoplasia in prostate of castrated mice (Bousset *et al*, Plos Biol 2020). LXRs are key players in immune response and can be pharmacologically manipulated with ligands to regulate genes implicated in immune anti-tumoral response. We therefore investigate the immune changes associated with LXR loss in preclinical models of PCa and focused our attention on dendritic cells (DCs). In a second part, we tested the ability of LXR ligands to modulate tumor growth and DCs functionalities both *in vivo* (*Pten*$^{pc-/-}$ model) and *in vitro* (THP-1 derived DCs).

We found that LXR DKO enhanced tumor growth, even when restricted to non-tumoral cells, in both genetically engineered (Pten $^{pc-/-}$) and RM-1 subcutaneous-graft model of prostate cancer. This phenotype was associated with profound alterations of tumor immune infiltrate, characterized by an enrichment in DCs in Pten $^{pc-/-}$ model. Moreover, in this model, pharmacological activation with the agonist GW3965 succeed to reduce both tumoral weight and DC infiltration. Conversely, in THP-1 derived DCs, LXR activation with GW3965 reduces *Cd80*, *MhcII*, *Ccr7* expression, while treatment with an inverse agonist increased their expression. These genes are implicated in both DC migration and maturation, suggesting that activation of LXRs may be deleterious for DCs functionality.

Together, these findings demonstrate that in Pten$^{pc-/-}$ PCa, LXRs are crucial regulators of DC activation and migration, key processes for effective T-cell priming. Further studies are ongoing to confirm these findings using DCs specific LXRs loss in RM-1 preclinical model. However, we have to assess that these observations can be extended to human PCa through LXR KO in THP-1 cells and analysis of immune infiltrate in patients' biopsies, in relation to the LXR pathway.

MACROPHAGES LIMIT BENIGN PROSTATE HYPERPLASIA DEVELOPMENT BY ENHANCING EPITHELIAL CELL PLASTICITY

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Background

Benign Prostate Hyperplasia is characterized by epithelial cell proliferation, stromal hypercellularity and immune infiltrates mainly composed of T lymphocytes and macrophages. We previously demonstrated that this phenotype is associated with an expansion of luminal progenitor cells (LSCmed) in Pb-PRL mice, a well-established BPH model. Luminal progenitors display an immunomodulatory signature and have been described to be associated with myeloid cell infiltration in prostate cancer. The aim of this study was to explore the role of macrophages in BPH development and epithelial cell plasticity.

Methods

RWPE1 and THP1 cells were used *in vitro* to investigate epithelial functions in response to macrophage conditioned media. Murine and patient-derived organoids were generated to explore progenitor capacities in the presence of macrophage-secreted factors. Finally, prostate macrophage profiling by spectral flow cytometry and macrophage depletion experiments were performed in Pb-PRL mice.

Results

We first demonstrated that macrophages are strongly enriched in the prostate of Pb-PRL mice. Spectral flow cytometry revealed that these cells mainly exhibit CD11c+, CD206+ and CD9+TREM2+ phenotype. *In vitro*, macrophage-conditioned medium limited epithelial cell proliferation while promoting luminal progenitor gene expression and transcriptomic signature. *Ex vivo*, pro-inflammatory macrophages enhanced murine and patient-derived organoid-forming capacities and limited their growth. Finally, macrophage depletion in Pb-PRL mice increased prostate weight and cell proliferation but reduced epithelial cell plasticity, as evidenced by a decreased proportion of LSCmed cells.

Conclusion

This study sheds light on a novel regulatory dialog between epithelial and immune cells in BPH. We demonstrated that macrophages limit epithelial cell proliferation while promoting epithelial cell plasticity during BPH pathogenesis. Our ongoing studies aim to elucidate the mechanisms by which macrophages influence epithelial phenotype in order to propose new therapeutic strategies based on these findings

Session V : Poster session

5

MET'CONNECT: A STRUCTURING ACTION TO ADVANCE THE UNDERSTANDING OF TUMOR CELL METABOLISM

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Tumor metabolism represents a fundamental area of research in oncology. A comprehensive understanding of cellular metabolism is essential for developing therapeutic strategies that lead to more effective treatments capable of overcoming resistance to therapy. Met'Connect supports projects that are directly related to tumor metabolism. This structuring initiative relies on state-of-the-art instruments that provide detailed insights into metabolic processes. Among the tools available on the platform are the Omnilog, the Seahorse, the YSI, and the hypoxia chamber. The Omnilog system enables phenotypic screening of cultured cells in the presence of various metabolites, allowing the identification of key metabolic pathways involved in cell proliferation. The Seahorse analyzer performs functional metabolic profiling by measuring mitochondrial respiration and extracellular acidification, the latter serving as a reflection of glycolytic activity. The YSI automated system quantifies glucose, lactate, glutamine, and glutamate levels in a 96-well format. In addition, hypoxic conditions can be simulated using two dedicated chambers that allow precise control of oxygen concentration. These experimental approaches are implemented to facilitate the rapid and optimized generation of results.

A jury evaluates the quality of the posters using mainly the following three criteria: clarity, self-explanatoriness and layout.

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FRANÇAISE
D'UROLOGIE


Pierre Fabre
Médicament


accord
Make it better


AstraZeneca


MSD
INVENTING FOR LIFE


Pfizer


astellas