BOOST YOUR PUBLIC-PRIVATE COLLABORATIONS WITH THE CANCEROPÔLE PROVENCE-ALPES-CÔTE D'AZUR

Book of Opportunities for Collaborative Research in Oncology

cancéropôle
Provence-Alpes-Côte d'Azur

le propulseur régional des recherches
et innovations anticancers

SOMMAIRE

Le Canceropôle Provence-Alpes- Côte d'Azur, le propulseur régional des recherches et innovations anticancers

TOUS POUR LE PATIENT !

Groupement d'intérêt public, le Canceropôle réunit et sert la communauté académique, scientifique, médicale et industrielle de Provence-Alpes Côte d'Azur. Notre mission : propulser les recherches et innovations anticancers, des découvertes fondamentales aux applications thérapeutiques.

1 région, 2 métropoles majeures, 8 piliers fondateurs

Les deux plus grandes universités de Provence-Alpes-Côte d'Azur
Aix-Marseille, Universite Côte d'Azur.

Les deux plus grands hôpitaux
l'Assistance publique-Hôpitaux de Marseille - le Centre hospitalier universitaire de Nice

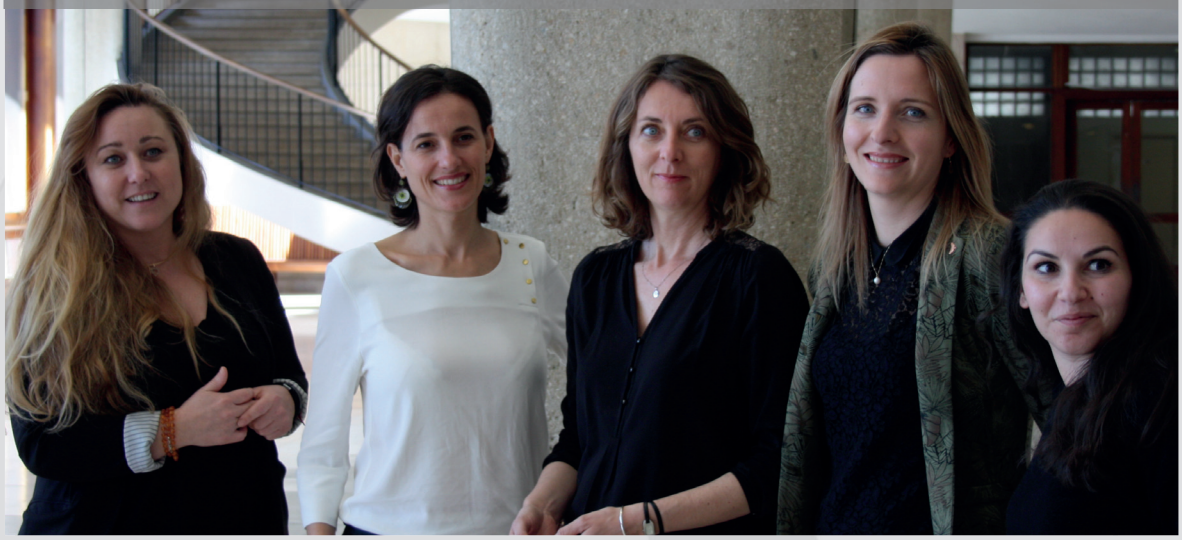
Les deux Centres de lutte contre le cancer
l'Institut Paoli-Calmettes à Marseille - le Centre Antoine Lacassagne à Nice

Les deux grands organismes nationaux de la recherche scientifique et médicale
CNRS, Inserm

« Le Canceropôle agit à toutes les étapes qui précèdent le soin. Les processus en jeu sont complexes et nécessitent une vaste communauté d'acteurs aux expertises très diverses. Notre rôle est d'aider ces expertises à mieux œuvrer ensemble. »

Clara Ducord
Directrice du Canceropôle

L'EQUIPE DU CANCEROPÔLE



Le Canceropôle anime, soutiens, accompagne les chercheurs et les équipes dans différentes disciplines pour accélérer l'avancée vers les thérapies de demain. Il favorise la maturation et le transfert des résultats de recherche vers la médecine et l'industrie, pour activer le développement de nouveaux outils, diagnostics et traitements.

LES PROPULSEURS DU CANCEROPOLE

> Le soutien financier des chercheurs, des cliniciens, des équipes par appels à projets compétitifs et cohérents.

> La mise en relation de la communauté : rencontres scientifiques, groupes de travail, création de réseaux d'experts...

> L'exploration des besoins, le déploiement et le financement de solutions collectives : mutualisation de technologies de pointe, partage de savoir-faire, compétences...

> L'appui à la (pré)maturation de projets à fort potentiel de transfert, via des cofinancements avec les cellules de valorisation ainsi que nos partenaires académiques et industriels.

> L'information des patients et usagers sur les avancées scientifiques et les essais cliniques.

UNE COMMUNAUTÉ RÉGIONALE DE TRÈS GRANDE VALEUR, UN ÉCOSYSTÈME D'EXCELLENCE INTERNATIONALE

"Le comité scientifique du Canceropôle représente les chercheurs et cliniciens de Provence-Alpes-Côte d'Azur, pour répondre à leurs besoins et soutenir leurs initiatives : développement de plateformes technologiques innovantes, demandes de financements et évènements, accompagnement dans la valorisation de projets de recherche, mise en réseau et structuration..."

Sophie Tartare-Deckert
Présidente du Comité Scientifique

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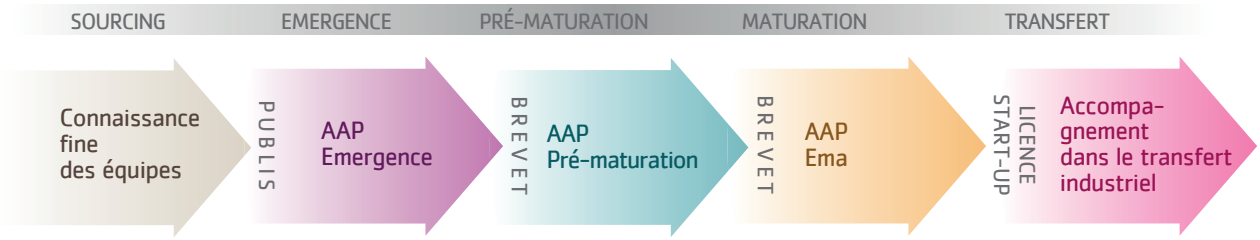
Le Programme EmA "Emergence et Accompagnement" pour booster vos collaborations public-privé en PACA

LE CANCEROPÔLE PACA DANS LA CHAINE DE L'INNOVATION

A chaque étape de la chaine de l'innovation le Canceropôle Provence-Alpes-Côte d'Azur propose aux équipes de recherche de la région et plus largement à la communauté scientifique spécialisée en cancérologie un accompagnement et des options de financement via ses appels à projets. Il s'appuie pour cela sur sa connaissance des acteurs du terrain et ses collaborations avec les structures régionales.



LE PROGRAMME EmA (EMERGENCE ET ACCOMPAGNEMENT)

Ce programme du Canceropôle Provence-Alpes-Côte d'Azur souhaite renforcer la compétitivité de la recherche en cancérologie menée en France, et plus particulièrement en région PACA, et des entreprises partenaires.

Les enjeux

A travers ce nouvel appel, lancé fin 2015 par le Canceropôle, l'enjeu est double : d'une part renforcer le lien entre la recherche et le monde économique, et d'autre part garantir le financement pluriannuel de projets valorisables en partageant le risque financier. Les projets financés pourront entrer dans une démarche de développement et de valorisation (collaborations public-privé, création de biotech, développements avec des groupes coopérateurs, etc). Le Canceropôle s'inscrit dans une démarche collaborative avec les principaux acteurs de la recherche et acteurs économiques en PACA existants ou en émergence (tels que les Biotech locales, nationales ou internationales, Marseille Immunopôle, les IDEX locaux, FHU, la SATT Sud-Est, Inserm Transfert, etc) pour répondre aux exigences

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du développement d'outils diagnostics ou produits thérapeutiques en cancérologie. La prise de risque financière, portée par le Canceropôle (200 à 300k€/projet), apporte un véritable effet levier aux programmes de recherche, plus à même de convaincre des co-financeurs de s'engager. Pour atteindre cet objectif ambitieux, le schéma de cet appel permet de mettre en place des partenariats sur-mesure « gagnant-gagnant », adaptés aux besoins des acteurs régionaux (industriels, structures de valorisation, IDEX, etc.)

Depuis le lancement d'EmA :

Dépôt des dossiers : au fil de l'eau

Financement du Canceropôle : 300 k€ max

Critère d'éligibilité : avoir un co-financement

16 projets soumis
95 experts contactés
6 projets retenus

4.1M€ engagés

1.4 M€ investis par le Canceropôle Provence Alpes Côte-d'Azur

2.7 M€ investis par les partenaires

SATT SUD-EST
ACCELERATING TECHNOLOGY TRANSFER

Advent France Biotechnology

innate pharma
the innate immunity company

Les retombées

La première édition de cet appel est un exemple de coopération réussie entre acteurs régionaux intervenant à différentes étapes du processus d'innovation et partageant des objectifs communs de soutien et valorisation de la recherche.
Depuis 2016, pour 1€ investi par le Canceropôle, 2€ sont apportés par les partenaires financiers. Ce sont ainsi 6 projets qui ont été financés pour plus de 4.1 millions d'euros, avec un investissement initial d'un peu plus de 1,4 millions d'euros apporté par le Cancéropôle PACA sur une période de 2 à 5 ans. Parmi les retombées attendues au niveau régional, nous pouvons citer le dépôt de brevets, le renforcement au niveau régional des relations entre recherche académique et industrielle, mais aussi la réalisation d'essais cliniques sur notre territoire (répondant à l'un des défis phares du Plan Cancer 3) et la création d'une start-up.

Mise en œuvre et suivi des projets

- Les projets retenus pour financement sont sélectionnés sur la base d'une évaluation externe réalisée par des rapporteurs de dimension internationale. L'évaluation se fait au regard de plusieurs critères parmi lesquels la qualité scientifique du projet, son caractère innovant et ambitieux, mais également l'impact des résultats attendus et du projet ainsi que son potentiel de valorisation du projet à l'issue du financement.
- Un Comité de Pilotage du projet est mis en place, composé du porteur de projet, un membre du Canceropôle, un représentant du ou des partenaires, et autres personnalités nécessaires en fonction des besoins du projet.

Success story du projet EmA :
La start-up Yukin Therapeutics est une SAS fondée par les chercheurs inventeurs, spécialisée en développement pharmaceutique, et basée à Biot (06). Yukin Therapeutics vise à utiliser ces inhibiteurs « first-in-class » de la kinase NIK sur des indications ciblées en oncologie. Par ailleurs, les chercheurs ont déjà obtenu des résultats prometteurs sur d'autres indications comme le cancer colorectal notamment. Yukin Therapeutics est accompagnée par son actionnaire principal, le fonds d'investissements en santé Advent France Biotechnology. La SATT Sud-Est, qui a transféré la technologie grâce à un programme de maturation, et un programme Emergence et Accompagnement (EmA) initié et piloté par le Canceropôle PACA, est entrée au capital de Yukin Therapeutics. Yukin Therapeutics a pour objectif de poursuivre le développement de ses composés en phases cliniques.

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DEVELOPMENT OF NOVEL IMMUNOTHERAPIES AGAINST EPITHELIAL CANCERS

PI : Fabienne Anjuere, Véronique Braud
Lab : IPMC, Sophia-Antipolis

1 SENTENCE PITCH

Decipher the functions of innate immune cells during epithelial inflammation and cancer development for the identification and validation of candidates for therapeutic intervention and local vaccination.

POTENTIAL APPLICATIONS

- Onco-dermatology
- Squamous cell carcinomas (skin and head and neck cancers)
- Other epithelial cancers

CONCEPT

- Need of new treatments to limit relapse
- Actual treatments (Surgery, radiotherapy)
- Our concept: development of local treatments to reprogram local effector and memory immunity

COMPETITIVE ADVANTAGES / BENEFITS

- Unique transcriptomic profiles of immune cells sorted from skin carcinomas obtained by the laboratory
- Strong expertise in anti-tumor immunity and mucosal immunology
- Combination of mouse and human studies : POC in vivo in mouse and in vitro on human cells

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Identification of candidates genes to reprogram innate immune cells
- Validation of selected therapeutic candidates to decipher mechanisms

IP SITUATION

None

PI : Fabienne Anjuere, Véronique Braud

Lab : IPMC, Sophia-Antipolis

KEY WORDS :
Carcinomas, epithelial cancers, innate immunity, local reprogramming, immune checkpoints

MAIN RESEARCH TOPICS :
- Innate immunity (focus on dendritic cells, neutrophils, innate lymphoid cells including natural killer cells)
- Oncogenic signaling
- Immuno-oncologie (focus on epithelial cancers)

LAB STRENGTHS :
- Strong expertise in epithelial immunology, innate immunity
- Development of ad-hoc mouse models
- Access to biological samples (Coll. CAL, IUFC, Nice)
- State of the art technical approaches (proteomics, genomics, flow cytometry, imaging)

KEY PUBLICATIONS :

- Braud *et al*, Nature, 1998
- Anjuere *et al*, Blood, 1999
- Hervouet *et al*, Muc. Immunol, 2014
- Germain *et al*, Oncoimmunology, 2015

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Single domain antibody-based multispecific construct for the manipulation of immune synapses

PI : Patrick Chames
Lab. : CRCM

1 SENTENCE PITCH

We develop innovative multispecific constructs able to recruit and active innate immune cells within the tumor microenvironment.

POTENTIAL APPLICATIONS

Antibody-based immunotherapy of non-inflamed tumors

CONCEPT

- Generation of agonistic single domain antibodies (sdAbs) against activating receptors such as CD16 and NKG2D as well as blocking sdAbs against checkpoint inhibitors such as SIRP , CD96, TIGIT
- Combination as multispecific molecules using proprietary format, with serum half life extension strategies

COMPETITIVE ADVANTAGES / BENEFITS

- Unique expertise in single domain antibodies (CRCM platform awarded by IBISA label since 2012
- 20 years expertise in antibody engineering
- Development of relevant 3D tumor spheroid in vitro models infiltrated by human effector cells

Contact Cancéropôle Provence Alpes Côte-d'Azur : canceropole-paca@univ-amu.fr - Tél : 04 91 32 47 00

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Development of relevant in vivo models
- Preclinical characterization of multispecific antibodies

IP SITUATION

2 patents. Co-development or licensing opportunities will be considered.

PI : Patrick Chames

Lab : CRCM, Marseille

KEY WORDS :
Immunotherapy Single domain antibodies

MAIN RESEARCH TOPICS :
- Multispecific antibodies
- Modulation of innate synapses

LAB STRENGTHS :
- Nanobody platform
- Strong expertise in antibody engineering
- Strong expertise in phage display
- Relevant in vitro models

KEY PUBLICATIONS :

- Scholler P et al Nat Comm (2017) 8(1) 1967.
- Kruwel et al Sci Rep (2016) 6: 21834.
- Nevoltris et al ACS Nano (2015) 9(2): 1388-1399.
- Turini et al Oncotarget (2014) 5(14): 5304-5319.
- Rozan et al Mol Cancer Ther (2013) 12(8): 1481-1491.

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The proteasome-associated deubiquitinating enzymes are novel therapeutic targets in melanoma

PI : Marcel Deckert
Lab : C3M/U1065/TEAM 11

1 SENTENCE PITCH

Targeting the proteasome-associated deubiquitinating enzymes induces melanoma cell death and overcomes resistance to MAPK-targeting therapies in vitro/in vivo

POTENTIAL APPLICATIONS

Onco-Dermatology

CONCEPT

- Deubiquitinating enzymes (DUBs) have been associated to multiple diseases, including cancer.
- Advanced cutaneous melanomas show high plasticity, metastatic potential and resistance to treatment. New targeted therapies and immunotherapies are limited to a subset of patients and relapses often occur.
- Targeting cancer proteostasis is a new strategy to overcome resistance to MAPK-targeting therapies in melanoma

COMPETITIVE ADVANTAGES / BENEFITS

- Targeting the ubiquitin-proteasome system in solid tumors (ie melanoma) is not yet clinically developed
- POC : in vitro and in vivo with favorable preclinical profile
- Selectivity of targeting proteasome-associated DUBs, compared to proteasome inhibitors (ie velcade)

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

Identification and characterization of novel drugs targeting proteasome-associated DUBs and cancer proteostasis

IP SITUATION

1 patent

PI : Marcel Deckert

Lab : C3M/U1065/TEAM 11

KEYWORDS :
Melanoma, Cancer Biology, Ubiquitine Proteasome System, MAPK Resistance, Deubiquitinase, Pharmacology

MAIN RESEARCH TOPICS :
- Onco-dermatology
- Cancer proteostasis
- Cell death

LAB STRENGTHS :
- Expert in cell biology & Signaling
- Identification of new druggable targets
- Development of in-house ad-hoc pre-clinical models
- Collaboration with clinicians from the CHU Nice for development of human studies

KEY PUBLICATIONS :

- Didier et al. 2018 Mol Cancer Ther 17 :1416
- Hamouda et al. 2016 J Exp Med 213:1705
- Tichet et al. 2015 Nat Commun 6:6993
- Prod'homme et al. 2015 J Clin Invest 125:1396
- Fenouille et al. 2011 Oncogene 30 :4887
- Essafi et al. 2011 Mol Cancer Ther 10:37
- Levaot et al. 2011 Cell 147:1324
- Baudot et al. 2009 Oncogene 30 :4887

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Toward a new plasma profiling optical tool for cancer diagnosis and monitoring

PI : Francois DEVRED
CO-PI : Emeline TABOURET
LAB : INP – PINT, Marseille

1 SENTENCE PITCH

Develop a universal high-throughput easy to use and cost-effective method that gives a disease signature based on the denaturation profile of plasma, allowing reliable diagnosis and monitoring of all cancers

POTENTIAL APPLICATIONS

- Monitoring of cancer progression
- Differential/early diagnostics of cancers and other diseases
- Identification of new cancer biomarkers

CONCEPT

- Every cancer has specific diagnosis method (when it exists) some of which can be very invasive or come too late
- We propose to follow the change of optical properties of plasma upon heat denaturation to characterize disease specific signature
- The constitution of a plasma calorimetric profiles atlas of cancers and development of Artificial Intelligence-based toolbox (pattern recognition and machine learning) will then be used for clinical interpretation of the profiles

COMPETITIVE ADVANTAGES / BENEFITS

- Proof of principle achieved for glioblastoma by identification a specific plasma signature
- High throughput instrument easily transferable to clinics
- No need to have a prior knowledge of the molecular biomarkers of the disease

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

▪ Development of the plasma calorimetric profiles atlas of cancers ▪ Development of Artificial Intelligence-based toolbox by data scientists ▪ Evaluate the prognostic potential of the plasma signature of glioblastoma ▪ Extend to all types of cancers

IP SITUATION

1 patent. Co-development or licensing opportunities will be considered.

PI : Francois Devred
CO-PI : Emeline Tabouret
Lab : INP–PINT, Marseille

KEY WORDS :
Diagnosis, Plasma, Cancer interactome, Biomarker, Glioblastoma

MAIN RESEARCH TOPICS :
- Diagnostic and prognostic applications of biophysical methods
- Molecular mechanisms of action of anticancer drugs

LAB STRENGTHS :
- Glioblastoma expertise
- Access to Glioma sample collections and patients data
- Unique calorimetric platform (PINT) and expertise
- Tight University-Hospital environment

KEY PUBLICATIONS :

- Tsvetkov et al. 2018 Oncotarget
- Tabouret et al. 2017 Neuro Oncol
- Figarella-Branger et al. 2016 Neuro Oncol

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Detection of lesions induced by inter-strand crosslinks (ICLs) based chemotherapeutic drugs.

PI : Christophe LACHAUD
LAB : CRCM, Marseille

1 SENTENCE PITCH

The detection of the lesions is essential to measure the level of repair of the cells and organs. We aim to use this new generation molecules to adjust treatment in patients.

POTENTIAL APPLICATIONS

▪ Sensitivity quantification ▪ Blood disorder prevention ▪ Screen for inhibitors of ICL repair

CONCEPT

▪ ICLs are highly toxic for replicating cells and are used heavily to treat cancer. The use of ICL is limited mainly because of the severity of the side effects (anaemia, immunodeficiency) and an increased probability of developing acute myeloid leukaemia (AML).
▪ All ICLs-inducing drugs and all patients are not equal regarding their probability to induce or develop AML.
▪ Exploiting these differences will help us in characterizing how ICLs affect blood cells; how they drive the transformation into leukaemia as well as how does the cells prevent these events.

COMPETITIVE ADVANTAGES / BENEFITS

▪ Expertise in the field of ICLs repair in mice models
▪ New detectable derivate of molecules used in clinic or clinical trials
▪ Proprietary novel unpublished approaches that are at the state of the art of the field
▪ Collaboration with pathologists from Institut Paoli Calmettes cancer center to develop the most relevant in vivo models

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Identification of inhibitor to improve efficiency of treatment
- Quantification of unrepaired lesions to identified the patient at risk of developing strong side effect

IP SITUATION

In the process of patenting new detectable molecules

PI : Christophe Lachaud

Lab : CRCM, Marseille

KEY WORDS :
Acute Myeloid Leukemia (AML), chemotherapy, alkylating agents

MAIN RESEARCH TOPICS :
- Understand how chemotherapy induces AML using alkylating agents on mice model
- Identify genes of predisposition for the development of leukaemia following chemotherapy
- Identify new targets to sensitize cancer to alkylating agent by characterizing alternative ICL repair pathways

LAB STRENGTHS :
- Use of mouse models to characterize the function of ICL repair proteins
- Development of novel approaches for the quantification of ICLs in vivo
- Optimum clinical and research environment for the study of the relation between DNA repair and cancer
- Access to patients samples

KEY PUBLICATIONS :
- Lachaud et al. NSMB 2016
- Lachaud et al. Science 2016
- Lachaud et al. G&D 2016
- Munoz et al. Plos one 2014
- Lachaud et al. JCS 2014

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http://www.ciml.univ-mrs.fr/fr/science/lab-bertrand-nadel/introduction

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Integrative structural & chemical biology

PI : Xavier MORELLI
CO-PI : Yves COLLETTE
LAB : CRCM, Marseille

1 SENTENCE PITCH

We aim to identify, to understand, to validate and to target protein-protein interaction interfaces critically involved in tumor cell signaling, with the purpose of transferring therapeutic and pharmacological targets into preclinical and clinical development programs in oncology.

POTENTIAL APPLICATIONS

Cancer therapy

CONCEPT

- Medical need in hematological cancers (and others)
- Innovative approaches targeting protein-protein interfaces
- High-throughput screenings (HTS) coupled to chemo-informatics to accelerate hit-to-lead developments in PPIs

COMPETITIVE ADVANTAGES / BENEFITS

- Unique PPI-focused chemical library ready for HTS
- Unique integrated HTS/Cheminformatics platform in France
- Strong knowledge in PPIs interfaces & inhibition

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

▪ HTS targeting PPIs ▪ Epigenetics: Bromodomains / methyltransferases ▪ Preclinic model / validation

IP SITUATION

WO2007066018 / WO/2009/063412 (abandoned) ▪ WO2017021435 ▪ WO2017114843

PI : Xavier Morelli
CO-PI : Yves Collette
Lab : CRCM, Marseille

KEY WORDS :
Protein-protein interaction (PPI), bromodomain proteins

MAIN RESEARCH TOPICS :
▪ Protein-Protein Interaction ▪ Drug Design

LAB STRENGTHS :
▪ HTS Facility state-of-the-art ▪ Structural Biology (X-Rays) ▪ Cheminformatics Platform ▪ Medicinal Chemistry Platform ▪ Chemical Biology ▪ Preclinic Platform

KEY PUBLICATIONS :
10 PubChem PMID (* corr. Author)
▪ 30908019* ▪ 29883107* ▪ 29127277* ▪ 28972073 ▪ 28617811* ▪ 28416471 ▪ 27219844* ▪ 26980515* ▪ 26754771 ▪ 26735842*

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The Lymphoma Single Cell Atlas

PI : Bertrand NADEL
CO-PI : Sandrine ROULLAND
LAB : CIML, Marseille

1 SENTENCE PITCH

Use integrative single-cell analysis and proprietary bioinformatics pipelines to define an unprecedented "Functional Lymphoma Identity Card"

POTENTIAL APPLICATIONS

Personalized medicine and/or immunotherapy:
- Identify innovative therapeutic targets
- Identify biomarkers of response to treatment

CONCEPT

▪ Unmet medical needs for Lymphoma : ▪ Address issue of recurrent & chemoresistant relapses; ▪ Optimize management & differential therapy of responding vs. high-risk patients ▪ Gene expression profiling, based on averaged signals from bulk tumor, has failed to deeply remodel lymphoma stratification and to provide biomarkers/therapeutic targets ▪ Single-cell technology allows to address functional dynamics, intra-tumoral heterogeneity & cancer cell plasticity, and to identify the presence of small yet impacting subclonal populations (e.g. Cancer Precursor Cells seeding relapses)

COMPETITIVE ADVANTAGES / BENEFITS

▪ Proof-of principle achieved for follicular lymphoma ▪ Proprietary bioinformatics pipelines ▪ Translational research operative through CALYM/LYSA(RC) (retrospective collections, prospective trials) ▪ Preclinical in vivo models for drug validation

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

▪ Extend to other lymphoma subtypes (double-hit, CLL, DLBCL) ▪ Integrated analysis: single-cell (tumor + microenvironment) & confocal imaging ▪ Screen on clinical trials (functional analysis of response to therapy, biomarkers)

IP SITUATION

None

PI : Bertrand Nadel
CO-PI : Sandrine Roulland
Lab : CIML, Marseille

KEY WORDS :
Lymphoma, Integrative single cell, Bioinformatics

MAIN RESEARCH TOPICS :
▪ Understand (epi)genetic mechanisms of leukemo- & lymphoma-genesis ▪ Identify new therapeutic targets & predictive/theranostic biomarkers

LAB STRENGTHS :
▪ Lymphoma & leukemia expert ▪ Member of Carnot Institute on Lymphoma (CALYM) consortium ▪ Single-cell technology ▪ CRISPR/Cas9 functional genome-wide screens ▪ Bioinformatic pipelines ▪ Access to unique human sample collections ▪ à la carte in vivo preclinical models (retroviral infection, KO/KI, PDX) for target validation & drug testing

KEY PUBLICATIONS :

▪ Roulland et al, JCO 2014 ▪ Sungalee et al, JCI 2014 ▪ Milpied* et al, Nat Immunol 2015 ▪ Milpied et al. Nat Immunol 2018

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NIK inhibitors and cancer. Potentiating the response to immune checkpoint blockers with new innovative compounds.

PI : Thierry Passeron – Laboratory : C3M, Nice
PI : Rachid Benhida – Laboratory : ICN, Nice

1 SENTENCE PITCH

A new class of NIK inhibitors restore a senescence program in cancer cells and potentiate the treatment with immune checkpoint blockers in treated tumor cells.

POTENTIAL APPLICATIONS

▪ Melanoma ▪ Colon cancer ▪ Solid tumors : lung cancer and all cancers with increased EZH2 expression

CONCEPT

▪ In melanoma, metastatic therapies, such as anti-PD-1 immunotherapy, will extend treatment duration and replace generic chemotherapies. But too few patients respond to them (10% to 57% depending on cancer type and treatment combinations).
▪ The new class of NIK inhibitors we develop targets the non-canonical-NF-kB pathway, a key regulator of the EZH2 oncogene.
▪ The inhibition of EZH2 by NIK inhibitor restores a senescence program in treated cancer cells and induces the secretion of a cytokine secretome that activates CD8 T cells and NK and stimulates M1 macrophages polarization.

COMPETITIVE ADVANTAGES / BENEFITS

▪ Allosteric inhibitor of NIK
▪ Potentiate immune checkpoint blockers.
▪ Demonstrated to be effective *in vivo* in melanoma and colon (10 mg/kg/d) and active in most solid cancers *in vitro.*
▪ High selectivity of our compounds confirmed by two kinase profiling
▪ Good tolerance *in vitro and in vivo.*

Contact Cancéropôle Provence Alpes Côte-d'Azur : canceropole-paca@univ-amu.fr – Tél : 04 91 32 47 00

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Synthesis and characterization/Optimization of derived compounds with improved solubility.
- Regulatory preclinical development and toxicology test in order to go to phase I study (melanoma).

IP SITUATION

Pathway and compounds protected (3 patents). Co-development or licensing opportunities will be considered.

PI : Thierry Passeron
Lab : C3M, Nice
PI : Rachid Benhida
Lab : ICN, Nice

KEY WORDS :
Melanoma, colon cancer, lung cancer, immune checkpoints inhibitors, EZH2, Non-canonical NFkB pathway.

MAIN RESEARCH TOPICS :
- Melanoma
- Colon cancer
- Lund cancer

LAB STRENGTHS :
- Clinical and fundamental experts in the field of melanoma and pigmentary disorders
- Highly translational researches (access to patients sample collections for melanoma and vitiligo)
- Strong collaborations with Nice Chemistry Institute (co-development of patented compounds)
- in vivo experiments in rodents
- Phase 1 to 3 clinical studies

KEY PUBLICATIONS :

- M Cerezo *et al,* Cancer cell, 2016
- De Donatis GM *et al,* Oncogene, 2016
- Regazzetti C *et al,* J Invest Dermatol. 2015
- Regazzetti C *et al,* J Invest Dermatol. 2015b

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Identification of a biomarker able to predict the response to anti-CD20 based therapy and to identify patients who will benefit the most to metabolic inhibitors

PI : Jean-Ehrland Ricci
Laboratory : C3M, Nice

1 SENTENCE PITCH

We identify a way 1) to predict poor outcome upon anti-CD20 based therapies of B-lymphoma patients and 2) to identify patients that will benefit the most of metabolic inhibitors.

POTENTIAL APPLICATIONS

- Companion test for the use of metabolic inhibitor in cancers
- Predictive marker to the response to anti-CD20
- Hematological diseases and autoimmune affections

CONCEPT

- The estimated market size for non-Hodgkin lymphoma is 100 M€.
- Unmet medical needs : inability to predict the response to metabolic inhibitors or the resistance to anti-CD20 based therapies at diagnosis.
- The expression of our identified protein/mRNA at the diagnosis will closely determine the probability that a patient will poorly respond to anti-CD20 based therapies. It is also a unique enrolment biomarker able to identify patients with the greatest potential response to metabolic inhibitors.

Contact Cancéropôle Provence Alpes Côte-d'Azur : canceropole-paca@univ-amu.fr - Tél : 04 91 32 47 00

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COMPETITIVE ADVANTAGES / BENEFITS

▪ No equivalent as a predictive marker for the response to metabolic inhibitors in cancer patients. ▪ Unique predictive markers of the response to anti-CD20 based therapies ▪ Marker validated in preclinical models as well as with several hundred of patient samples and finally tested in clinic on 9 patients.

AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Metabolic inhibitor in oncology (not only for NHL)
- New anti-CD20 antibodies
- Alternative therapies for patients presenting a resistance to R-CHOP
- IHC or genomic screening tests

IP SITUATION

3 patents (predictive marker of the response to : anti-CD20, metabolic inhibitors, mTOR inhibitors). Co-development or licensing opportunities will be considered

PI : Jean-Ehrland Ricci
Lab : C3M, Nice

KEY WORDS :
Metabolism, Metabolic Inhibitors, Anti-Cd20, B-Lymphoma, other cancer types

MAIN RESEARCH TOPICS :
▪ Multispecific antibodies ▪ Modulation of innate synapses

LAB STRENGTHS :
▪ Study of the role of energetic metabolism on B-lymphoma response to chemotherapies ▪ Metabolism inhibition as an innovative way to sensitize tumor cells to treatment ▪ Modulating tumor cell metabolism to enhance anti-cancer immune response.

KEY PUBLICATIONS :

- Chiche J et al, Leukemia. 2015 ▪ Meynet O et al, Blood. 2013
- Jacquin MA et al, Cell Death Differ. 2013
- Bénéteau M et al, PNAS. 2012 ▪ Meynet O et al, Leukemia. 2012

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http://www.unice.fr/c3m/index.php/research-teams/jean-ehrland-ricci/

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Instantaneous label free histology label free imaging microscope and endoscopes

PI : Hervé RIGNEAULT
LAB : INSTITUT FRESNEL

1 SENTENCE PITCH

We develop stimulated Raman imaging and phase imaging, in microscopy and endoscopy, which allows the instantaneous assessment of cancer tissues

POTENTIAL APPLICATIONS

Intraoperative histology
Metabolic histology

CONCEPT

▪ Classical histology requires intensive labor and time (24h) to access cancer diagnostics ▪ We develop innovative stimulated Raman and phase microscope/endoscope that provide histology images in few minutes only ▪ These innovative technologies should provide instantaneous histology imaging on fresh tissues samples, in an intra-operative context

COMPETITIVE ADVANTAGES / BENEFITS

▪ Instantaneous histology is made available ▪ Raman imaging can also address metabolic imaging to provide cancer metabolic assessment on cells and tissues ▪ Endoscopic imaging provides living tissue cancer imaging

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

▪ Cancer cell and tissue imaging ▪ Cancer cell metabolism imaging

IP SITUATION

10 patents in the field of label-free tissue imaging

PI : Hervé Rigneault

Lab : Institut Fresnel, Marseille

KEY WORDS :
OPTICAL IMAGING

MAIN RESEARCH TOPICS :
▪ Label free imaging of tissue ▪ Label free histology ▪ Metabolic imaging

LAB STRENGTHS :
▪ Optical instrumentation and engineering ▪ Optical microscopy ▪ Optical endoscopy ▪ Phase imaging ▪ Nonlinear imaging

KEY PUBLICATIONS :
▪ Sarri et al. Fast stimulated Raman imaging for intraop rative gastro-intestinal cancer detection. arXiv:1902.08859
▪ Lombardini A. et al. High-resolution multimodal flexible coherent Raman endoscope. Light: Science & Applications vol7, Article number: 10 (2018)

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Synthesis and Characterization on new antiproliferative compounds efficacious in various melanoma tumor models including BRAF/MEK inhibitor / immunotherapy resistant models and other solid tumors.

PI : Stéphane ROCCHI
LAB : C3M, Nice

1 SENTENCE PITCH

New anti-melanoma compounds to found new alternative therapies to overcome primary and/or acquired resistances to current therapies.

POTENTIAL APPLICATIONS

▪ Melanoma therapies for patients resistant to current therapies (Targeted therapies and immunotherapy) ▪ Cancer therapy (liquid and solid tumors)

CONCEPT

▪ Highly unmet medical needs metastatic melanoma (5-year survival rate at stage IV of 15-20%). Immunotherapy gives 15 to 30% of responses. Anti-BRAF treatments trigger resistance within a couple of months and there is no efficient alternatives. ▪ Products in development are mainly BRAF/MEK/ERK and PI3K/AkT/mTOR inhibitors. ▪ New products targeting other signaling pathways are needed to efficiently address melanoma resistance.

COMPETITIVE ADVANTAGES / BENEFITS

▪ POC: in vitro and in vivo with favorable preclinical profile ▪ New strategies to address melanoma resistance problem

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

Project 1 : Compounds triggering endoplasmic reticulum stress exert anti-melanoma effects and overcome BRAF/MEKinhibitors and immunotherapyresistances. Project 2: New biguanide derivatives that induce melanoma cell death in AMPK-dependent and independent manner.
Objectives for : Projects 1 & 2 : Hit to Lead optimization, Safety and tolerability studies. Project 2 : Target and off-target studies.

IP SITUATION (PATENT, EXISTING LICENSES, ETC)

2 patents. Co-development or licensing opportunities will be considered.

PI : Stéphane Rocchi
Lab : C3M, Nice

KEY WORDS :
Melanoma Therapy, Other Cancers Therapies, AMPK, BRAF inhibitor resistance, Endoplasmic Reticulum Stress

MAIN RESEARCH TOPICS :
▪ Melanoma ▪ New AMPK activators ▪ New Biguanide derivatives ▪ Thiazole Benzensulfonamides (TZB) compound family ▪ Endoplasmic Reticulum stress activators

LAB STRENGTHS :
▪ Clinical and fundamental experts in the field of melanoma and pigmentary disorders ▪ Highly translational researches (access to patients sample collections for melanoma and vitiligo) ▪ Strong collaboration with Rachid Benhida at the Nice Chemistry Institute (co-development of 2 patented compounds) ▪ Specifics technics in house or easily accessible

KEY PUBLICATIONS :

M Cerezo et al, Cancer cell, 29 (6):805–819, 2016. A Lehraiki et al., Cell discovery. 1, 15030, 2015. A. Lehraiki et al., JID, 134(10):2589-97, 2014. Cerezo et al, Molecular and Cellular Therapeutics, 12(8):1605-15, 2013. T. Tomic et al., Cell Death and Disease, 1;2:e199, 2011.

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Development of monoclonal therapeutic antibody targeting metastatic function of SPARC

PI : Sophie Tartare-Deckert
Laboratory : C3M, Nice

1 SENTENCE PITCH

We (i) identified a novel targetable pathway used by melanoma cells to disseminate at distant sites and (ii) provided a rationale and mechanistic basis for targeting SPARC/VCAM1 interaction to prevent metastasis.

POTENTIAL APPLICATIONS

Cutaneous melanoma and others cancers expressing SPARC (Glioma & Breast Cancers)

CONCEPT

Metastatic propensity is a hallmark of melanoma and not all patients are candidates and responders to the current targeted therapies and immunotherapies.
We propose to develop novel therapeutic approaches preventing the establishment of metastatic foci by targeting the interaction of SPARC, a secreted factor of the matricellular protein family, which circulating levels correlate with metastatic melanoma, with the endothelial VCAM1 receptor (Nat Commun 2015).

COMPETITIVE ADVANTAGES / BENEFITS

- Transfer of our basic discoveries in melanoma to the clinic facilitated by the existing interactions with the Nice University Hospital.
- New strategy targeting circulating metastatic cells and extravasation.
- No SPARC function-blocking antibody available to date.

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

Development and characterization of SPARC/VCAM1 function-blocking human monoclonal antibodies against melanoma for clinical application.

IP SITUATION

None

PI: Sophie Tartare-Deckert

Lab : C3M, Nice

KEY WORDS :
Melanoma, Sparc, Vcam1, Monoclonal Antibody, Anti-Metastatic Therapy

MAIN RESEARCH TOPICS :
- Onco-dermatology
- Oncogenic signaling
- Metastatic cascade
- Tumor microenvironment

LAB STRENGTHS :
- Expertise in melanoma
- Access to biological resources
- Experimental models and settings
- Innovative tools for screening tumorigenic pathways
- Translational research

KEY PUBLICATIONS :

- Olvedy, M. et al. J. Clin. Invest. 2017; in press.
- Tichet, M. et al. Nat. Commun. 2015;6:6993.
- Prod'homme, V. et al. J. Clin. Invest. 2015;(4):139.
- Fenouille, N. et al. Oncogene, 2011;30(49):4887.
- Fenouille* N, Puissant* A, et al. Cancer Res. 2010;70(23):9659.

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New Chemical Entities (NCE) For Glioblastoma Treatment

PI : Thierry VIROLLE
LAB : iBV, Nice

1 SENTENCE PITCH

Target GSCs with new small molecules to repress stemness properties and double the effectiveness of chemotherapy.

POTENTIAL APPLICATIONS

▪ Glioblastomas ▪ Other solid tumors with resistance due to stem cells

CONCEPT

▪ Differentiating therapy : the goal is to force GSCs to exit their stemness program, thus losing their stemness and tumorigenic properties

COMPETITIVE ADVANTAGES / BENEFITS

▪ Novel family of small molecules
▪ More than doubling temodal's effectiveness (x2,5)
▪ No toxicity of the drug candidates alone
▪ Innovative mode of action: targetting cancer stem cells by blocking their stem-like properties
▪ Stop glioblastoma stem cell clonal properties and growth in vitro and in vivo
▪ No toxicity observed at 50 µM on primary normal cells: neuronal, hepatic, kidney…
▪ New strategy to address glioblastoma resistance problem by specifically targeting cancer stem cells properties

Collaboration opportunities

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Phase one clinical trials
- Combining with immunotherapy

IP SITUATION (PATENT, EXISTING LICENSES, ETC)

Patent in preparation

PI : Thierry Virolle

Lab : iBV, Nice

KEY WORDS :
Glioblastomas, Small Molecules, Resistance, Cancer Stem Cells

MAIN RESEARCH TOPICS :
▪ Brain tumors ▪ Glioma stem cell plasticity and functional intra-tumor heterogeneity

LAB STRENGTHS :
- Team composed of researcher and clinicians
- Strong expertise in brain tumors, glioma stem cells and gene expression

KEY PUBLICATIONS :
▪ Debruyne et al, 2018, Oncogene ▪ Fareh et al, 2017, Cell Death and Dis ▪ El-Habr et al, 2017, Acta Neuropathol ▪ Sakakini et al, 2016, J Biol Chem ▪ Burel-Vandenbos et al, 2013, Neuro Oncol ▪ Nayernia et al, 2013, Biomaterials ▪ Turchi et al, 2013, Stem Cells ▪ Fareh et al, 2012, Cell Death and Diff

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Validating the use of new positive modulators of p2rx7 to induce tumor regression

PI : Valérie VOURET-CRAVIARI
LAB : IRCAN, NICE

1 SENTENCE PITCH

I uncovered that the purinergic receptor P2RX7 restrained colon tumor growth challenged by chronic inflammation and I proposed that P2RX7 is essential to support anti-tumor immune responses and/or to restrict neoplastic formation and tumor growth. In collaboration with chemists, we developed chemical compounds able to enhance P2RX7 activity in order to boost its anti-tumor property

POTENTIAL APPLICATIONS

Immuno-oncology

CONCEPT

▪ Many tumors, such as lung cancers, remain resistant to treatments, leading to premature death of the patient ▪ New therapeutic approaches are needed to improve patient outcomes ▪ We designed small molecules to promote P2RX7's anti-tumor therapeutic effect

COMPETITIVE ADVANTAGES / BENEFITS

▪ We developed small-molecules displaying increased P2RX7-dependent cell activity and no toxicity in the absence of P2RX7 or its ligand. Through this strategy, we sought for chemical compounds harboring high P2RX7-dependent selective anti-tumor activity in the ATP rich tumor environment and low overall toxicity in normal tissues. ▪ Combine to anti PD-1, the lead compound cures LLC tumor bearing mice

Collaboration opportunities

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AXES FOR DEVELOPMENT OF COLLABORATIVE RESEARCH PROGRAMS

- Identification of molecular and cellular targets of the new patented compound
- Prepare the transfer to human clinic

IP SITUATION (PATENT, EXISTING LICENSES, ETC)

1 patent (EP 10831-01)

PI : Valérie Vouret-Craviari

Lab : IRCAN, NICE

KEY WORDS :
P2RX7, ATP, Onco-Immunology

MAIN RESEARCH TOPICS :
- Purinergic signaling
- Inflammation and cancer

LAB STRENGTHS :
- Facilities and Safety
- Available qualified Lab personnel
- Excellent platforms
- Interaction with clinicians

KEY PUBLICATIONS :

- Paul Hofman, et al. Cancer Research, 2015, 75:835
- Alexandre Bozecet al. Oncotarget, 2017, 8: 57174-8

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Faculté de Médecine - 27 Bd Jean Moulin - 13005 Marseille - Tél : +33(0) 4 91 32 47 00
www.canceropole-paca@univ-amu.fr - www.canceropole-paca.com