RESEARCH2BUSINESS ONCOLOGY MEETING : Pitchs de projets collaboratifs

Bioactive Coatings of Multiple-Well Culture Plates

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DESCRIPTION DE L'ACTIVITE
Biomedical engineering, Tissue engineering
Engineering of very thin surface coating of biopolymers and bioactive proteins and peptides (thickness in the nanometer and micrometer range), which play the role of biomimetic environments for cells to grow and form mini-tissues
Controlling the composition (polymer type), the stiffness and the bioacctivity (nature of the biomolecules trapped in the biomimetic film) of the biomimetic films
Automated process to deposit the biomimetic films in multiple-well cell culture plates has been patented
The film-coated microlates can be analysed at high content using conventional techniques (optical microscopies, microplate readers...)

PARTENARIAT RECHERCHE
Pharmaceutical company to provide and test their bioactive molecules (proteins or drugs) (of GMP grade)
Companies workiing on stem cell therapies: the biomimetic coatings can be used to prepare and specific stem cells in view of future therapies
Companies producing GMP-grade extracellular matrix proteins, polysaccharides and polypeptides
Academic labs who want to study specific cellular responses

DESCRIPTION DU PROJET
Cell culture is widely used for growing living cells artificially outside their natural environment under controlled physical conditions: to study cellular structures and functions, stem cell differntiation, to do molecular and genetic engineering as well as drug screening, commercial production of drugs and biologics.

To date, cell culture in vitro is performed in plates, flasks, dishes of different sizes that are made of stiff and synthetic materials (glass, polystyrene), which may bias the experimental results. In vivo, the cellular behavior is strongly influenced by the mechanical and biochemical properties of their microenvironment, namely their extra-cellular matrix (ECM). This soft ECM network is made of proteins and polysaccharides confining bioactive molecules, such as growth factors that provide biochemical signals modulating cellular functions. The challenge is to mimic this natural environment in vitro and to present these biochemical signals from softer substrates in order to control and study cellular processes.

We developed an innovative surface-coating of multi-well plates with advanced physico-chemical and biochemical functionalities. This surface-coating is made by self-assembly of biopolymers that mimics the natural extracellular matrix (ECM), providing a soft environment and biochemical signals (proteins, peptides, growth factors). Advantageously, our technology is flexible in terms of chemical composition, mechanical properties and bioactivity, compatible with automated liquid handling systems and microscopic analysis, high throughput thanks to multiple-well plate format.
Our innovative process will broaden the applications of coated plates in research and industry

MOTS-CLES
nanomedicine, health technologies, tissue engineering, biomimetisms, surface coating

MECACHIPS

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DESCRIPTION DE L'ACTIVITE
Mecachips develop culture plates for in vitro 2D cell culture that mimic the in vivo chemo-mechanical properties of almost all our tissues. Indeed, the Mecachips innovative and patented technology allows the elaboration of a soft and flat layer made of polyacrylamide hydrogel that can exhibits uniform or patterned elastic properties. Mecachips culture plates are pre-coated with proteins of the extracellular matrix and supports long time cell cultures without degradation nor modification of its mechanical and chemical properties. MecaChips culture plates are very easy to handle and ready-to-use, similar to plastic culture plates and are being developed in standard size and format. Mecachips culture plates are dedicated to (1) cell culture and cancer research, with the aim of offering cell culture conditions with mechanical features as close as possible to the pathophysiological features of animal or human tissues, (2) stem cells differentiation, to promote the emergence of physiologically relevant phenotypes and (3) drug discovery, in order to screen drugs in more physiological conditions so to raise the relevance of the hits and uncover new molecules more efficient in clinic. Indeed, studies reveal that responses derived from current assays are biased by the lack of mechanical physiological relevance of the in vitro culture device. Thus Mecachips culture plates will provide a new and more physiological microenvironment for cell culture and tests.

PARTENARIAT RECHERCHE
We are looking for a partnership with a Biotech or a CRO company able to drive a drug screening assay on Mecachips Culture Plates.

DESCRIPTION DU PROJET
Our organs are "soft", with rigidities span between few Pa and few tens of kPa. However, up to now, cell culture and cell tests performed in cancer research laboratories, pharmaceutical industries or screening platforms are mostly operated on plastic (or glass) dishes, which rigidities are about gigapascal (GPa), thus more than 1 6 times stiffer than our organs. This lack of in vivo relevance and mechanical physiology of the standard culture plates is a true limitation, as many studies have proved that the mechanical properties of the micro-environment deeply impacts almost every aspect of cell behavior (e.g. adhesion, spreading, migration, proliferation, differentiation) for a vast number of cell types. The Mecachips project fills this gap by developing a completely new generation of cellular culture plates that offer soft and biomechanical substrates for in vitro 2D cell culture and tests. The MecaChips technology combines an unprecedented micron scale control of the plate mechanical properties with an independent control of the surface chemistry thus assuming the chemo-mechanical robustness of the culture environment. Unique is the ability of MecaChips culture plates to mimic physiological mechanical heterogeneities of the extracellular matrix on a single plate!
Mecachips is currently in incubation with the SATT Grenoble Linksium and currently located at the Laboratoire des Technologies de la Microélectronique, in the Minatec campus (CEA Grenoble).

MOTS-CLES
in vitro cell biology, elastic culture plates, physiological in vitro cell culture

Development of In Vivo Tumor Models Resistant to Treatments

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DESCRIPTION DE L'ACTIVITE

Antineo accelerates and optimizes preclinical development of anticancer agents. We carry out Proof-of-Concept studies to reveal the antitumor efficacy of your compounds. We provide the best preliminary in vitro and ex vivo data to refine in vivo experimental designs.
Our scientific team is able to advice you on:

- the best choice of indication
- the best model
- the reference treatment to use as comparison
- the reference treatment to combine with your compound

Our clients benefit from animal facilities and personnel fully and immediately authorized for PK, toxicity and antitumor efficacy studies on mice and rats.
Our most sought-after activities are:

- our expertise in the development of therapeutic antibodies: deciphering of the mechanistic action in vitro, ex vivo (ADCC, ADCP, CDC etc) and in vivo (ADCC, CDC, test of bispecific antibodies without the costly use of humanized mice).
- our fully characterized models of acquired resistance to reference treatment (anti-CD2 , ADC anti-Her2, anti-CD38, anti-PD1/PDL1 etc). Such models allow to test in vivo innovative therapeutics designed for resistant tumors, in a clinically relevant context.
- Antineo also develops bespoke resistant models upon request.

With its expertise and reactivity, Antineo will accelerate the development of your anticancer agents

PARTENARIAT RECHERCHE

We would like to integrate and offer our expertise within public funded projects such as PoC, EuroStars or FUI call for projects, for co-development with R&D teams developing new cancer treatments, either in combination or in competition with reference drugs. Antineo's partners will benefit from high-end model development technology, years of experience and top-level expertise in several oncology diseases for the development and the use of relevant and reliable pre-clinical resistance models.

DESCRIPTION DU PROJET

A large number of cancer patients will initially respond to medical therapy before suffering relapse with resistant disease. In order to develop novel active and original therapies it is therefore necessary to test novel agents in clinically relevant resistance models.
Our models are developed to be resistant to gold standard therapies, which reflect the clinical situation in which novel agents will be analyzed in the scope of phase II clinical trials. Importantly we perform molecular and phenotypic characterization of our resistance models in comparison to the parental sensitive models. While all preclinical models suffer from limitations, our approach provides our customers with a unique opportunity to evaluate their agents in models which are closely related to clinical situations of resistance.
So far, Antineo has obtained models resistant to chemotherapy and/or immunotherapy. Those models, CDX or syngeneic, are representative of various indications. We therefore have the know-how to develop, in the frame of a consortium agreement, a variety of resistant models

MOTS-CLES

oncology, resistance, immuno-oncology

CellenONE™ X1, the Single Cell Dispenser

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DESCRIPTION DE L'ACTIVITE

Cellenion has developed a new tool, CellenONE™ X1, for single cell isolation based on deterministic delivery of ultra-low volume via automated image analysis. CellenONE™ X1 can be compared to an automated liquid handler producing picodrops (each drop is a few hundreds of picoliters), able to monitor live if the next drop formed will contain a single cell and dispense only those drops containing single cell onto a define target. Thus, about 1 cells can be isolated in less than 4 minutes, a 384wp can be filled in ~15minutes. The rigorous control of the presence of one and only one cell per drop allows our deterministic (as opposed to statistic for most competing technologies), high throughput tool to be the only one on the market to deliver 1 % of single isolated cell in customer defined labware.

Major competitive advantages of CellenONE™ X1 are numerous:

1. Developed as an open platform: any type of sample (cells, particles, biologicals) and any labware/consumable can be used as source and target.
2. Ideally suited for isolation of single cells from rare samples given that isolation can be undertaken from just a few µL of sample with outstanding recovery rates up to >95%.
3. Allow isolation of cells within tiny droplets hence limiting background signals in single cell analysis.
4. The expertise developed at Cellenion is broad: clonal selection of transformed/transfected cells, isolation of cells from human samples, rare sample enrichment, NGS applied to single cells...

PARTENARIAT RECHERCHE

We are looking to partner with:

1. Research and medical teams specialized in cancers (new therapeutic target, mechanisms of drug resistance, companion test, cell therapy development, monitoring of patients, ...)
2. Teams or companies working in the field of NGS for technical development and miniaturization on specific technologies (scChIP-Seq, G&T-Seq, MALBAC, DR-Seq, SUPeR-Seq, Quartz-Seq, CEL-Seq, FRISCR Sequencing, scATAC-Seq, scBS/scWGBS, scM&T-Seq, scRRBS, Hi-C/3C-Seq, …)

DESCRIPTION DU PROJET

The single cell is the fundamental operative unit of a cancer. Single cells are genetically and epigenetically different depending on their environment (proliferating or quiescent, in the primary tumor mass or disseminated elsewhere, vascularized or not…). Most of current studies on cancer cells look at averages over cell populations, typically limiting observations to small variations. Single-cell analyses provide the ultimate level of resolution in the quest for a fundamental understanding of cellular processes such as cancer. Historically, this quest has been hampered by technological shortcomings that we hope address.

Our aim at Cellenion is to participate in the development of single-cell studies. By introducing CellenONE™ X1 on the market, we make single-cell isolation easier and more reliable. Using Cellenion's R&D and engineering resources together with this technology we would like to support the development of advanced methods in the field of oncology and precision medicine. One way we could contribute to a collaboration could be by offering the use of our single cell technology for proof of concept studies or by participating in the preparation of complex projects involving challenging technological developments.

MOTS-CLES

single cell, oncology, precision medicine, immunology, immunotherapies, personalized medicine, transcriptomics, genomics, big data, sequencing, RNAseq, bioinformatics

Infiltrative Glioma Detected by Fast Field Cycling NMR: A Nuclear Magnetic Resonance Technology of Low and Variable Magnetic Fields

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DESCRIPTION DE L'ACTIVITE

My research consists on the development of MRI methods for neuroscience applications in preclinic and in clinic in particular for brain tumors, but other pathologies and animal models are occasionally studied. It consists in establishing the relations between the multi-parametric NMR signal and the molecular and cellular characteristics of the biological tissue, its physiology and pathophysiology processes. It relies on the understanding of the NMR signal and its interaction at micro and nanometer scale. The methods use endogenous NMR parameters but also take advantage on the use of paramagnetic and super-paramagnetic probes. Methodological developments also concern NMR signal simulations (such Monte Carlo simulation of water diffusion on numerical models of brain microstructure) and mathematical NMR signal modelling (such the pharmacokinetics of contrast agents in tumors). Innovative MRI techniques for diagnostics and treatment monitoring are developed to study and characterize the microstructure and the microvasculature of brain tumors during their development. Most MRI methods using the properties of contrast agents for quantitative perfusion and methods using microscopic diffusion tensor for imaging white matter alteration and tumor cell migration are well established. I focus on new developments, like: molecular MRI for pH mapping, cellular MRI for tumor therapy and Fast-Fields Cycling NMR and MRI (FFC-NMR/MRI) for molecular dynamic characteristics

PARTENARIAT RECHERCHE

Clinicians, scientist and physicians specialists in breast cancer, brain cancer and cancer in general

DESCRIPTION DU PROJET

Fast Field Cycling Nuclear Magnetic Resonance (FFC-NMR), which measures relaxation times T1 at different magnetic fields (T1-dispersion profiles) in low regime (< 1T) is used in physics and chemistry to characterize the molecular dynamics of materials. Here in this project, our aim is to highlight the role of FFC-NMR in medicine. This project is a part of the European H2 2 project (IDentIFY: Improving Diagnosis by Fast Field Cycling MRI) that includes the development of basic theory which will improve our knowledge of Nuclear Magnetic Resonance relaxation phenomena and will provide quantitative and precise data analyses, in turn providing FFC "biomarkers" that will be directly useable by clinicians. Our first aim is to perform FFC-NMR experiments on human tissue samples, obtained from tissue banks and during surgical procedures and to carry out FFC-MRI studies on patients. Only by performing measurements on human tissues can the robustness of the FFC disease biomarkers be determined. This is a vital first step in validating the clinical effectiveness of FFC-MRI after completion of the technical upgrades above compared to existing diagnostic techniques.Purpose

MOTS-CLES

fast-field-cycling NMR, fast-field-cycling-MRI, relaxometry, cancer, glioma, T1-dispersion curve, power model, quadrupolar peaks

Development of New RF Sensor for Early Diagnosis of Breast Cancer

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DESCRIPTION DE L'ACTIVITE

Dr. Latifa Fakri-Bouchet received her B.S., M.S., and her Ph.D. degrees (1996) in engineering physics, specialized in electronics and RF instrumentation, from the University Claude Bernard Lyon 1, Lyon, France.
From 2 to 2 14, she was Associate Professor at the University Claude Bernard Lyon1. Since 2 15, she is currently Associate Professor (Hors Classe) at INSA of Lyon and affiliated with the ISA Laboratory (Institute of Analytical Sciences – UMR 528), Villeurbanne, France.
Her expertise is within Electronic, RF instrumentation: coil and microcoil for NMR (MRI and MRS) biomedical applications (Alzheimer Disease) and RF sensors for RF/Microwave Interaction with Biological Tissues and application for Early Diagnosis of Breast Cancer.

PARTENARIAT RECHERCHE

To find academic partners with expertise in algorithmic field, signal processing and imaging reconstruction, same as private partners for technological transfer, industrial scholarship (CIFRE). Also to find different partners to apply for national or European project calls.

DESCRIPTION DU PROJET

Our project focuses on the development of the RF sensors, and more particularly on the development of the RF sensor array configuration that plays an important role in MI systems. Our RF sensor array system is chosen in order to improve resolution and to enhance the sensitivity and selectivity with new innovative and flexible microstrip antennas that might allow one of the first possible underwear-integrated, optimal signal, low cost, and easy-use prototypes.Breast cancer is the most commonly diagnosed cancer among women [1] According to the American Cancer Society, approximately 252,71 breast cancer deaths are expected in 2 17 in the United States [2].
An early diagnosis will increase the survival chance among patients and they will require less expensive treatment [3]. Many breast imaging techniques were been studied and are commonly used for diagnosing early-stage breast cancer, like Mammography, Contrast-enhanced (CE) digital mammography MRI, ultrasonography, PET, CT and biopsy. However all these techniques are expensive methods that require trained people and have respective limitations [4] that imply complementary investigation.
Over the past years, several Breast Cancer Non-Invasive Detection Techniques have been started to develop using different equipment and materials, confirming that one of the most efficient ones is Microwave Imaging (MI).
MI techniques can be grouped as passive and active approaches. Passive MI uses radiometry to measure the temperature differences between normal and malignant tissues Active one concerns microwave tomographic and radar-based MI. It measures the dielectric properties (DPs) contrast between healthy tissue and malignant tissue in the high-MHz to low-GHz regime. Active MI is an emerging mammography technique for diagnosing breast cancer.

[1] Mohebian, M.R. et al. Comput. Struct. Biotechnol. J. 2 17.
[2] www.breastcancer.org
[3] Migowski, A.et al. Cienc. Saude Coletiva, 2 15.
[4] Abel, E.J. et al. BJU Int. 2 13.

MOTS-CLES
breast cancer; radio frequency sensor, microwave-sensing, microwave imaging.

Accélérer la recherche grâce à une plateforme de recherche collaborative: Seintinelles.

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DESCRIPTION DE L'ACTIVITE

Au-delà des besoins financiers, les chercheurs ont des besoins fondamentaux en ressources humaines pour trouver des volontaires susceptibles de participer à leurs études. Bien souvent, l'inclusion de volontaires est laborieuse ce qui peut mettre en péril la faisabilité de certaines recherches. La mission de Seintinelles consiste à accélérer le temps du processus de recherche grâce à une collaboration plus étroite entre citoyens et chercheurs via la 1ère plateforme de recherche collaborative dédiée à tous les cancers en France. Le recrutement de volontaires se fait sur www.seintinelles.com. L'animation de la communauté, principalement par email et via les réseaux sociaux, la création d'outils facilitateurs de la collaboration volontaires-chercheurs de même que l'administration de questionnaires en ligne, de modules de sciences participatives et de conférences sont organisés par les Seintinelles pour renforcer ce lien. Les projets mis en ligne sur seintinelles.com sont toujours validés au préalable par les autorités législatives classiques (CCTIRS, CNIL, CPP si nécessaire). Chaque projet est également soumis au comité scientifique des Seintinelles, dont le rôle est d'une part d'évaluer la pertinence scientifique de l'étude ainsi que sa faisabilité dans le cadre de la plateforme.

PARTENARIAT RECHERCHE

Dans une logique de promotion de la recherche communautaire et d'une forme de démocratie sanitaire, l'association Seintinelles vise d'une part à **impliquer davantage les citoyens dans la recherche** dès la conception même des études, et leur faire bénéficier plus rapidement de ses avancées. L'association et les chercheurs partenaires s'engagent en effet à communiquer les résultats obtenus à l'ensemble de la base de données. D'autre part, l'objectif de l'association est de **mettre à disposition des chercheurs des outils innovants permettant d'optimiser leurs processus de recherche**: le système informatique permettant d'encoder des questionnaires sur mesure, une base de données de plus de 20 000 citoyens volontaires, des communications régulières par newsletters et sur les réseaux sociaux, une responsable communication dont la mission est de donner de la visibilité aux projets de recherche, autant auprès de la base de données qu'auprès d'un réseau de partenaires et des médias. Un projet d'application mobile est également en préparation, afin d'avoir accès à des données jusqu'ici impossible à collecter à grande échelle.

DESCRIPTION DU PROJET

Quatre ans après le lancement du site, 21 000 citoyens (hommes et femmes, malades ou non) se sont déjà inscrits sur Seintinelles. Une vingtaine d'études ont été menées dont certaines sont toujours en cours, parmi lesquelles : Prédisposition à la douleur après une mastectomie, Entourage de personnes malades, Effets secondaires des traitements du cancer du sein, Etude sur le cancer de la prostate, Impact du cancer sur les conjoints, Etude sur les implants PIP.

Les recrutements (de quelques dizaines à plusieurs milliers de volontaires) peuvent s'effectuer en quelques heures ou quelques jours seulement : 1000 volontaires en 24h pour un questionnaire sur le dépistage et la prévention, 20 personnes pour des entretiens qualitatifs en 48h là où on aurait mis plusieurs mois avec des processus classiques de recrutement.

L'objectif global vise à recruter et animer une communauté de 50 000 citoyens d'ici 3 ans, et de mettre en œuvre une quinzaine d'études par an. Le processus même de mise en place de la plateforme Seintinelles, sa démarche et ses questionnements scientifiques, éthiques et épistémologiques animent le conseil scientifique des Seintinelles et donneront lieu à une production scientifique parallèle.

ADDomer: A New Technology for the Immunotherapy of Cancer

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DESCRIPTION DE L'ACTIVITE
We address the challenge of a prophylactic vaccine to combat cancer such as melanoma. We have developped a novel synthetic protein scaffold, ADDomer, that we recently patented. ADDomer is a bio-similar based on a dodecahedral superstructure derived from human adenovirus penton base protein. ADDomer is uniquely suited for displaying up to 180 copies of peptide or protein epitopes and provides for adjuvant-free vaccination. Moreover, ADDomer can be produced in very large quantities, is ultrastable and has no cold-chain requirements.

PARTENARIAT RECHERCHE
We are seeking for academic or industrial partners having expertise in the immunotherapy field. Our goal would be to validate our ADDomer vaccine technology in animal models bearing cancer. Tumour Associated Antigens (TAAs) or neoantigens could be inserted in the ADDomer. Ideally, both the immune response triggers by our platform against the antigens and the prophylactic response would be studied by animal challenges.

DESCRIPTION DU PROJET
We have recently brought the ADDomer proof of concept in another topic. Indeed, a Chikungunya virus epitope displayed on ADDomer was able to trigger a strong immune response against this epitope, in absence of adjuvant, thus validating our versatile technology. We would like now to broaden the applications of ADDomer by adressing immunotherapy of cancer. For this, TAAs will be inserted in the ADDomer scaffold (preliminary data were obtained with OVA system) and we are seeking for partners to assess the efficiency of the immune response and the therapeutic effects in cancer models.

MOTS-CLÉS
vaccine, immunotherapy, TAAs, nanoparticle, patented