Internship supervisor and Host laboratory

Centre de Recherche en Cancérologie de Lyon, 28 rue Laennec 69008 Lyon
Director : Alain PUISIEUX
Team atip/avenir **« Inflammasome et cancer**,», headed by Virginie Petrilli
http://www.crcl.fr/110-Inflammasome-et-cancer.crcl.aspx?language=fr-FR

Titre du projet/ Research Project title :

Study of the NLRP3 inflammasome function in cancer.

Description du projet/Project Description :

Activation of the innate immune system triggers an inflammatory response that is crucial for pathogen clearance and tissue repair. Pathogen- and Damage-Associated Molecular Patterns (PAMP and DAMP) are detected by a variety of Pattern Recognition Receptors (PRR) including the cytosolic receptor NLRP3. Upon PAMPs or DAMPs recognition NLRP3 triggers the assembly of a molecular platform named inflammasome. Inflammasomes control the activation of caspase-1, the enzyme responsible for the maturation of 2 major proinflammatory cytokines (IL-1b and IL-18) and the induction of an inflammatory cell death.
Deregulated inflammation is responsible for several pathological conditions including cancer. In fact, most solid tumors are infiltrated with inflammatory cells that promote tumor progression by secreting various factors. The team “inflammasome and cancer” is a new CRCL team that studies the link between inflammasome activation and tumor development especially in the lung. The project will require the following techniques: tissue culture of human epithelial cells and mouse macrophages, transfection, Western blot, Real-Time PCR, immunofluorescence, flow cytometry.

Training Position: Ultrasound plasmids delivery and cells assembly within hydrogels

Tissue engineering aims at developing constructs composed of scaffold, cells and signaling proteins to replace or help in the repair of damaged tissues, or to generate in-vitro tissue models for example of tumors. Hydrogels, which are 3D networks of hydrophilic cross-linked polymers chains, are commonly studied as scaffolds materials. One of the current limits of current techniques is the difficulty to develop a vascular network within the gels, necessary to study cell-microenvironment interactions, in particular to study tumor angiogenesis. One option is to provide signaling cues to cells that will further develop new blood vessels (angiogenesis). This can be achieved by regulating gene expression of engineered cells, or by delivering signaling molecules such as growth factors. Moreover, cells can be assembled within the hydrogels, in lumen-mimicking structures, to promote vessels formation.

The aim of our currents studies is to develop an acoustic levitation platform allowing the assembly of cells within hydrogels in a simple and cost-effective manner. We are also aiming at combining this approach with focused ultrasound to locally deliver heat into the material, in order to spatially regulate the expression of therapeutic transgenes under the control of a heat-shock promoter, therefore allowing patterning protein expression within the scaffold.

The aim of the training period will be to participate in the development of this platform and associated ultrasound technology. Some of the objectives are to determine optimum formulation of constructs made of lipoplexes/fibrin/cells for optimum cell transfection and to test ultrasound as a source to induce localized heat-shock for spatially controlled gene expression. Methods used will include ultrasound models and experimentation and *in vitro* protocols (e.g. cell culture, microscopy, immunohistochemistry).

This work will be conducted at the Laboratory of Therapeutic Applications of Ultrasound (LabTAU) in Lyon, which belongs to the network of French National Institutes of Health and Medical Research (INSERM). This project is supported by the excellence laboratory initiative LabEx DEVweCAN, which unites eleven teams (biologists, pharmacologists, and physicists) of the highest potential and scientific ambition to realize projects of international importance in the field of cancer development and targeted therapies.

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Prodrug Platforms for Light Triggered Release of Chemotherapeutic Agents

Host: Institut des Technologies Avancées en sciences du Vivant

Mentors: Nathalie M. Pinkerton and Stefan Chassaing

MISTI France - Summer 2014

ITAV

L'Institut des Technologies Avancées en sciences du Vivant (ITAV) is an interdisciplinary, CNRS affiliated institute focused on basic and translational cancer research located in the Toulouse Oncopole. ITAV hosts several academic labs ranging in research interests from green chemistry, chemical biology, image analysis, to fundamental cancer biology, as well as three technology platforms – chemistry, imaging and nanotechnology. The dynamic and collaborative environment at ITAV will make for a wonderful internship experience. For more information on ITAV, please visit the institute website: http://www.itav-recherche.fr

Project Description

One of the difficulties in cancer treatment is the off-site toxicity of therapeutic agents and the resulting side-effects. These toxicities limit the dose and frequency of therapeutic administration, which can lead to resistance and tumor rebound. To improve targeted delivery of cytotoxic drugs and to minimize off-target cytotoxicity, nanocarriers (NC) that accumulate in solid tumors *via* the enhanced permeation and retention effect have been developed. These vehicles add spatial specificity, but do not address temporal control of the drug release. To add triggered release capabilities, we have developed a near-infrared (NIR) light sensitive prodrug platform that is encapsulated into NCs. Upon illumination with NIR-light, the platform releases chemotherapeutic drug from the NC into the tumor tissue. The next step involves expanding the types of chemotherapeutic agents that can be easily linked to the prodrug platform to create a universal platform. In this context, the student will be involved in developing and optimizing the synthesis of a variety of prodrug constructs and evaluating their photochemical/photophysical properties in solution and in NC form.

Skills and Experience

We are looking for a student with prior research experience in small molecule synthesis, purification and characterization. We expect the student to be self-motivated, creative, responsible and detail-oriented. Strong communication skills and the ability to work well with others are critical.

Toulouse

Toulouse, known as la Ville Rose because of its unique brick buildings, is a beautiful and vibrant city. There is an abundance of restaurants, cafes and shops. Delicious fresh produce, cheese and meat can easily be found in the many markets, most notably the Victor Hugo, Carmes and St. Aubin markets. For weekend excursions, a quick train ride can take you to the beach, the mountains or to famed Cathar castles.

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Evaluation of Light-Responsive, Therapeutic Nanocarriers in Microtumors

Host: Institut des Technologies Avancées en sciences du Vivant

Mentors: Nathalie M. Pinkerton, Stefan Chassaing and Valérie Lobjois

MISTI France - Summer 2014

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Skills and Experience

We are looking for a student with prior research experience in human cell culture, microscopy and image analysis. We expect the student to be self-motivated, creative, responsible and detail-oriented. Strong communication skills and the ability to work well with others are critical.

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