

## Lyonbiopôle and CLARA join forces on “Infections & Cancer” research

The CLARA cancer research cluster and the Lyonbiopôle competitive cluster formed a partnership in 2006. Complementing each other, the two networks have a common field of action: virology and cancer.

For CLARA, the research theme Infections and Cancer is one of the priority initiatives of ProCan, the French cancer center program. The collaboration between CLARA and Lyonbiopôle also falls within the scope of CLARA's Proof of Concept Program. This program consists in funding innovative projects with strong potential for exploitation and industrial transfer, the aim being to apply research outcomes.

human immunodeficiency virus (Kaposi's sarcoma), Epstein-Barr virus (Burkitt lymphoma and nasopharyngeal cancer), *Helicobacter pylori* (stomach cancer), as well as certain parasites such as schistosoma (bladder cancer).

### Agenda

March 8<sup>th</sup> to 11<sup>th</sup>, 2009  
BioVision, Lyon

March 9<sup>th</sup> to 11<sup>th</sup>, 2009  
BioSquare, Lyon

March 30<sup>th</sup> and 31<sup>st</sup>, 2009  
FABS, Lyon

April 15<sup>th</sup> to 17<sup>th</sup>, 2009  
Bangalore Bio 2009, India

May 18<sup>th</sup> to 21<sup>st</sup>, 2009  
BIO Atlanta, United States

June 16<sup>th</sup> to 18<sup>th</sup>, 2009  
BioMed Israel, Tel Aviv

September 23<sup>rd</sup> to 25<sup>th</sup>, 2009  
EuroBIO, Lille

October 7<sup>th</sup> and 8<sup>th</sup>, 2009  
BioContact, Québec

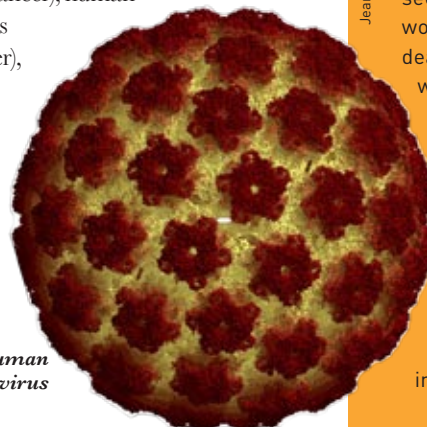
October 7<sup>th</sup> to 9<sup>th</sup>, 2009  
BioJapan, Tokyo

### Cancer: a Public Health challenge

Cancer is a leading cause of death in the world, responsible for 7.9 million deaths in 2007, representing 13% of the worldwide mortality rate. Cancer results from the modification of a single cell, caused by external forces or inherited genetic factors.

Among the external agents, certain viruses, bacteria or parasites may contribute to the onset of cancer.

Examples of infectious pathogens associated with certain cancers include hepatitis B and C viruses (liver cancer), human papillomavirus (cervical cancer),



Human Papillomavirus

### Key figures

#### Liver cancer:

Every year, 560,000 new cases are diagnosed worldwide, with approximately 653,000 deaths annually. Liver cancer is the third cause of mortality in men. During 2005 in France, with over 5,000 new cases of liver cancer every year, hepatitis B virus (HBV) and hepatitis C virus (HCV) caused 4,000 to 5,000 deaths, the majority of them (79%) among men.

#### Cervical cancer:

Cervical cancer killed more than 250,000 women in 2005, in majority in developed country. Cervical Cancer, which is the second most frequent cancer among women, will cause around 25% additional deaths in the next ten years, in accordance with World Health Organization (WHO).

Almost all cervical cancers (99%) can be traced to a genital infection with human papillomavirus (HPV). Seventy percent of these infections are linked to two oncogenic HPV types (16 and 18). If left untreated, the lesions can develop into cervical cancer after 20 to 30 years, or in as few as 15 years following an HPV infection with high oncogenetic risk.

Jean-Yves Sgro 2004.virology.wisc.edu/virusworld

# CLARA: a key player in national policy to fight cancer

Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA) is a cancer research cluster founded 5 years ago after the French Cancer Plan (2003/2007) was launched by then-president Jacques Chirac. One result was a call for cancer research projects, representing a budget of €16.5 million over 4 years. Aimed at setting up technological and scientific infrastructures, this call for projects led to the creation of 7 regional or inter-regional cancer research clusters in France, one of which is CLARA. The Law of August 9, 2004, completed the infrastructure by creating the French National Cancer Institute (INCa).

CLARA's mission is to encourage innovative new research programs in oncology. It thus fosters synergy between researchers, clinicians and industrial players. Since 2005, CLARA has been managed by the Léa and Napoléon Bullukian Foundation, created in Lyon in 1986. Declared to be of public interest in October 2003, the Bullukian Foundation, in accordance

with its founder's wishes, promotes applied research in the medical field.

## 2007 marked a turning point in CLARA's development

INCa launched a new triennial call for projects focused on cancer research cluster, called ProCan 2007/2010, with a global budget of €26.5 million. ProCan aims to keep French cancer research clusters up-to-date in terms of their scientific strategy and to strengthen their technological capabilities, define new technologies and set out new scientific initiatives.

Six focus areas for cancer research have been defined at clara:

- I. Nanotechnology, Imaging and Cancer
- II. Infections and Cancer
- III. Nutrition and Cancer
- IV. Epidemiology, Human and Social Sciences (SHS), Patient Education and Organization of Care
- V. Therapeutic Targeting, Modeling and Clinical Research
- VI. Tumor Escape

## CLARA's governance and mission

CLARA is run by 4 committees:

**The Strategic Orientation Committee** defines CLARA's general positions and validates issues submitted to the deliberative assemblies.

**The Executive Committee** implements the decisions of the Strategic Orientation Committee, validates and distributes funding, and clarifies differences in funding rules.

**The Scientific Steering Committee** oversees CLARA's scientific management together with the Industrial Steering Committee, which represents industrial interests.

**The Development Committee** approves the roadmap and sets CLARA's orientations, drawing on expertise in institutional, clinical, fundamental, epidemiological and translational research. This committee aims at closely focusing the research of CLARA teams on academic-industrial partnerships.

## French National Cancer Institute (INCa)

INCa was created by the Public Health Law of August 9, 2004, within the framework of the Cancer Plan. It is part of a long-term national policy on fighting cancer. It aims to reduce the cancer death rate in France and improve quality-of-life for people suffering from cancer. To accomplish this, it applies an interdisciplinary strategy geared towards uniting, harmonizing and rallying participants and resources around common projects.

# Core Research Programs based on ProCan

CLARA currently has three core programs on Infections & Cancer axe II of ProCan coordinated by Fabien Zoulim et Patrice Marche:

**1) Joint program on Toll-like receptors (TLR) and natural immunity** coordinated by Massimo Tommasino (International Agency for Research on Cancer – IARC, Infections and Cancer Biology Group). **Objective:** bring together existing tools and techniques in the Rhône-Alpes and Auvergne regions on TLR and natural immunity, and generate any tools and techniques that prove necessary.

**2) Detailed study and targeting of telosomic dysfunctions and in the telomerase during virally induced carcinogenesis**, led by Eric Wattel (CNRS UMR 5537 - Claude Bernard University, Léon Bérard Center, Oncovirology and biotherapies). **Objective:** check gene regulation of the telosome and the hTERT promoter for diagnostic, prognostic and therapeutic purposes (development of potentially antineoplastic peptides).

**3) Platform for isolating primary human hepatocytes and hepatic progenitor cells**, led by Philippe Merle (INSERM U871 - Claude Bernard University, hepatology and gastroenterology department, Hôtel-Dieu Hospital, Molecular pathophysiology and new viral hepatitis treatments, Viral hepatitis B and C pathogenesis team, Virally induced hepatic oncogenesis). **Objective:** set up a platform for preparing and storing human hepatocytes from resection, and analyze the early stages of carcinogenesis.

# Collaborations between Lyonbiopôle and CLARA

The neighboring regions of Rhône-Alpes and Auvergne boasts between them several centers for excellence in molecular virology, mechanisms of virally induced oncogenesis, immune response and clinical research. Cooperations between these groups are facilitated by Lyonbiopôle and CLARA, but also by the Synergie Lyon Cancer Foundation (national thematic network for research and care) and the Finovi Foundation (national thematic network for advanced research), along with the International Agency for Research on Cancer (IARC), the Léon Bérard Center and the Albert Bonniot Institute...

Leveraging their common interests, Lyonbiopôle and CLARA collaborate by cultivating synergies to generate new projects and mobilize the various players in the area of Infection and Cancer. Their collaborations are organized around three themes:

## 1- Set up collaborative R&D projects

*Four Lyonbiopôle members are already taking advantage of this partnership through the CLARA Proof of Concept Program:*

### 1/ Truncated IL-6 as a natural inhibitor of IL-6: *in vivo* demonstration

**Objectives:** select a controlled system in order to produce tIL-6 batches, pursue tIL-6 characterization and generate *in vivo* data from animal models

**Industrial partner:** IDD Biotech (project initially backed by EUSA Pharma, ex-OPi)

**Academic partners:** Laurent Alberti, Léon Bérard Center (coordinator), INSERM U590, Hospices Civils de Lyon (HCL civil hospitals of Lyon), Claude Bernard University  
Service provider: PX<sup>3</sup>Therapeutics

### 2/ Targeted cancer therapy with TLR3 receptor agonists

**Objectives:** Proof of Concept in animals for use of a TLR3 ligand as a breast cancer treatment

**Industrial partner:** Innate Pharma  
**Academic partners:** Serge Lebecque, Hospices Civils de Lyon (HCL), Claude Bernard University

### 3/ Lymphos1: Study of TCR repertory to predict lymphocytopenia in patients with breast cancer

**Objectives:** validate the immunoprognostic tool ImmunTraCkeR® developed by ImmunID which, by analyzing the immunological repertoire, identifies patients with increased risk of mortality following chemotherapy.

This tool will directly enable clinicians to adjust chemotherapy type and dosage for immunodeficient patients and prescribe personalized alternative treatments for them.

**Industrial partner:** ImmunID  
**Academic partners:** Christophe Caux, Cytokines and cancer team: Léon Bérard Center/INSERM U590

### 4/ Developing a new therapeutic approach for treating hepatocellular carcinoma

**Objectives:** preclinical Proof of Concept for an innovative approach to treating hepatocellular carcinoma

**Industrial partner:** ERYtech Pharma  
**Academic partners:** Toufic Renno, UMR CNRS 5201, Jean-Yves Scoazec, INSERM U865

*Through calls for projects of the FUI (national fund to support applied collaborative research projects) and through OSEO programs in support of French SMBs, Lyonbiopôle has already accredited six Infections & Cancer projects, which also obtained public fundings.*

#### ADNA

Advanced diagnostics for new therapeutic approaches: aims to contribute to personalized medicine for infectious diseases, cancer and genetic diseases, by providing healthcare professionals with innovative tools in the area of biodiagnostics and new therapies  
**Participants:** bioMérieux, GenoSafe, Généthon, Transgene

#### ALPHA VAC

New therapeutic approach to fight HCV  
**Participants:** Flamel Technologies (project leader), Transgene, INSERM U823, Hôtel-Dieu Hospital (HCL), Grenoble university hospital, Geneva canton hospital, Vaudois University Hospital in Lausanne

#### BIO THERAPIC

Therapeutic solutions to fight hepatitis C  
**Participants:** Transgene (project leader), Epixis, Hospices Civils de Lyon (HCL), Grenoble university hospital, INSERM U823, CNRS

#### DEMINAP

Using Toll-like receptors (TLR) to detect inapparent microbes and their ligands for diagnostic and therapeutic purposes



## CLARA's Proof of Concept Program

Establishing Proof of Concept is a key step in health-related R&D projects, whether they involve a demonstration in animals (preclinical research) or in patients (clinical research). This level of validation gives projects good visibility and risk control, making them acceptable to the main funding entities, namely health industry firms and venture capitalists. Available public funding is primarily allocated to the upstream phases of academic research. As a result, the initial development and validation stages for Proof of Concept are difficult to fund in France.

In response to this situation, CLARA set up a support program for Proof of Concept projects. Its aim is to develop partnerships between academia and industry in Rhône-Alpes/Auvergne through innovative projects with strong potential for Proof of Concept and transfers to industry. In three years of operation, CLARA has selected 14 projects representing a budget of almost € 18 million, funded by local authorities (€4.8 million) and industry partners (€13 million).

**Participants:** Innate Pharma (project leader), bioMérieux, International Agency for Research on Cancer, Claude Bernard University

#### PLATINE

Creation of a European immunomonitoring platform

**Participants:** Innate Pharma, Transgene and ImmunID Technologies, INSERM U590 (Cytokines and cancer) and U851 (Immunity, infection and vaccination)

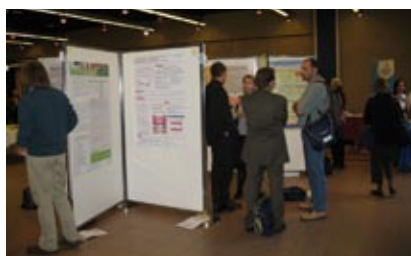
#### PRAVIC

Recombinant protein A for immunological and anticancer purposes

**Participants:** IDD-Tech (project leader), PX Therapeutics, Hospices Civils de Lyon, Léon Bérard Center

## 2-Mobilize networks of scientific and technological players

Lyonbiopôle, CLARA and their members participate in special events, dedicated to forging collaboration and developing networks, mainly through the following activities:



### a - CLARA's Scientific Forum

CLARA has been organizing Scientific Forums for four years. They are open to industrial players and health care professionals, to all cancer researchers but also to those working in human and social sciences. As a network of research teams, institutions and firms involved in cancer research, CLARA's objective is to make the regions of Rhône-Alpes and Auvergne a leading

European research site. The fourth edition of CLARA's Scientific Forum will take place March 24 and 25, 2009, in Archamps (Haute Savoie County). This event is an opportunity to present work in progress and to discuss the latest advances in fundamental, clinical and translational research. As part of Focus Area II of ProCan, a session on infections and cancer will be offered to foster exchange on recent developments in the field.



### b - Lyonbiopôle Partnering Days

Lyonbiopôle organizes its annual Partnering Days to get industry groups/SMBs/academics/clinicians working together, in view of new partnerships on technological and scientific issues and new R&D projects. During the course of the day, a selection of accredited and funded projects is presented and all projects are displayed in poster sessions. Thematic workshops and roundtable discussions take place in the afternoon. At the end of the 2007 Partnering Days, six workshops were selected and developed in detail in 2008: "Immune Response According to Age", "Predicting the efficacy of immune response", "Systems biology and pathogen/cell interactome", "Cellular tests for detecting viral infection", "Sepsis and markers of bacterial infection" and "Immunotoxicity". Partnering Days 2008, held October 24 in Grenoble, set new roundtable discussions, giving rise to new work groups and new collaborative endeavors.

## 3- Organize events on Infections and Cancer in 2009

### Joint meeting of the cancer centers CLARA, CGE and DKFZ on Infections and Cancer

A meeting on Infections & Cancer is being organized within the framework of the two Infections and Cancer networks: Cancéropôle Grand-Est (CGE) / Deutsches Krebsforschungszentrum (DKFZ), Joint Program in Applied Tumor Virology, and Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA), ProCan Focus Area II "Infections & Cancer", in partnership with the Finovi Foundation (national thematic network for advanced research). There will be three sessions: Diagnosis and treatment of virally induced cancers, Molecular mechanisms of virally induced carcinogenesis, Viral strategies for escaping immune response. This meeting will take place January 23 and 24, 2009, at the International Agency for Research on Cancer (IARC), 150 cours Albert Thomas in Lyon, France.

### Biennial Christophe Mérieux conference cycle: Viruses and Cancer

In winter of 2010 (January 17 to 19) "Viruses and Cancer" will be the focus of an international conference organized by the Mérieux Foundation at Les Pensières in Veyrier-du-lac (Haute Savoie county), in partnership with Lyonbiopôle, CLARA, the Finovi Foundation and the Synergie Lyon Cancer Foundation. This conference will offer international experts the chance to discuss the latest discoveries in the area of viruses and cancer.

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