

# Cancer Vaccine Collaborative

...a systematic, coordinated,  
global effort toward the creation  
of therapeutic cancer vaccines.



LUDWIG  
INSTITUTE  
FOR  
CANCER  
RESEARCH

“You won’t know how to vaccinate  
until you know how to immunize.  
And you won’t know how to immunize  
until you know how to monitor.”

-Lloyd J. Old, M.D.  
Director, Cancer Vaccine Collaborative

## The Cancer Vaccine Collaborative

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The CVC is an innovative partnership between two not-for-profit institutions, each with a long and distinguished history in the field of cancer immunology. The Cancer Research Institute (CRI) and the Ludwig Institute for Cancer Research (LICR) have committed themselves to taking responsibility for translating their laboratory discoveries into effective cancer therapies. The establishment of the CVC, a network of eminent scientists and clinicians at leading research and medical centers around the world, is a visible manifestation of this shared commitment.

The CVC employs a unique academic organizational structure that plans, sponsors, and conducts early-phase clinical trials to test the potential therapeutic benefit of research findings made by both organizations. A committee of scientists and clinicians from CRI and LICR works closely with select investigators at other leading institutions throughout the world to design the studies. CRI provides funding for the research components of the trials, including personnel, laboratory equipment, and the establishment of typing and monitoring laboratories. LICR provides funding, expertise in immunology, protocol design and development, the process development and production of clinical reagents, and the clinical trials infrastructure, including data management and regulatory compliance.

## Cancer Vaccines

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There is a great expectation that cancer vaccines will offer advantages over conventional cancer treatments such as chemotherapy and radiotherapy. Vaccines are likely to produce fewer and milder side-effects as they specifically target cancer cells only.

An ideal cancer vaccine would induce a strong and sustained immune response against a cancer antigen that is expressed only on cancer cells. Thus identifying an antigen is the first step in developing an effective cancer vaccine. The Cancer Antigen Discovery Collaborative (CADC), another joint CRI and LICR effort, convenes an international group of scientists to identify and characterize cancer antigens to which cancer vaccines can be targeted. A number of promising cancer antigens, including NY-ESO-1, MAGE-3, NY-BR-1, SSX-2, NY-CO-58, and MELAN-A, are often found in certain cancer types, including melanoma, and breast, prostate, lung, colon, ovarian, and bladder carcinomas, and were discovered by LICR investigators and by members of the CADC. The CADC continues to identify and feed potential cancer antigens into the CVC pipeline of clinical discovery (see diagram of CADC/CVC Process).

The ideal immune response to a cancer vaccine would be ‘integrated,’ meaning that all components of the immune system, CD8+ T cells, CD4+ T cells, and antibodies, are generated to target the antigen, leading to the destruction of the cancer cells. Therefore the development of an effective vaccine requires the ability to monitor both T cell and antibody responses to a defined antigen. In this respect, the successful development of robust, sensitive, and specific monitoring methodologies lies at the heart of the CVC.

The standardized monitoring employed by the CVC enables the comparison of single vaccine variables in simultaneous trials at many clinical centers. Variables being compared in the CVC vaccine trials include: the constitution of the antigen (protein, peptide, viral vectors, or DNA), the method, frequency, and intensity of antigen delivery, and the addition of adjuvants or immunostimulatory compounds (chemicals that enhance the immune response) (see diagram of Trials in Progress). The CVC approach of systematically testing different vaccines in parallel is without peer in academia and industry.

# CANCER ANTIGEN DISCOVERY COLLABORATIVE

Discovery

Characterization

Immune  
Response

Target

# CANCER VACCINE COLLABORATIVE

CLINICAL STRATEGY  
DEVELOPMENT

Agent  
Production

Protocol  
Development

Vaccine

CLINICAL TRIAL  
CENTERS

Trial

Immunological  
Monitoring

Clinical  
Response

ANALYSIS &  
STRATEGY  
REFINEMENT

## Clinical Trials Model

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The current view of translating scientific discoveries into clinical therapies imposes discrete roles on academia and industry. Academia generates the discovery; industry develops it into a product. Too frequently the clinic door is the line of demarcation between these separate domains.

The clinical trials discovery model employed by the CVC differs significantly from this traditional paradigm, and is the result of the pioneering academic partnership between CRI and LICR.

### Opening up the clinic door...

First, laboratory and clinical research are closely integrated during early-phase CVC clinical studies, allowing the novel discoveries made during these trials to be incorporated into future vaccine strategies.

### Scientific, rather than profit-driven, control of clinical trials...

The CVC's commitment to early-phase clinical trials includes: producing clinical-grade study agents in LICR's own biological production facilities, or obtaining them through collaborative agreements with commercial partners, preparing and submitting regulatory documentation, and ensuring that the trials are conducted under internationally recognized and approved safety, ethical, and scientific standards.

### Coordinated, systematic, standard-monitored, parallel...

Trials are conducted at multiple clinical centers, each supported by a laboratory, and each applying standardized techniques for immunological monitoring and clinical evaluation. This model allows an efficient and rapid comparison of many vaccine variables through their simultaneous and equivalent evaluation at different centers.

LICR and CRI believe that this distinctive model, unique in academia and industry, is essential to achieve the ultimate aim of creating effective human cancer vaccines.

# Trials in Progress

			Preclin.	Phase I	Phase II	
<b>Protein</b>	NY-ESO-1 + ISCOM	Melanoma	→→→→→			CVC Australasia
	NY-ESO-1 + CHP	Prostate Breast	→→→→→			CVC Asia
	NY-ESO-1 + CpG	Prostate	→→→→→			CVC Europe
	MAGE-3 + QS21/MPL	NSCLC	→→→→→			CVC N. America
	MAGE-3 + QS21/MPL + CpG	NSCLC	→→→→→			CVC Europe
<b>DNA</b>	NY-ESO-1 + rVaccinia + rFowlpox	Melanoma Bladder	→→→→→			CVC Europe
	NY-ESO-1 + rVaccinia + rFowlpox	Ovarian	→→→→→			CVC N. America
	NY-ESO-1 + PowderJect	NSCLC	→→→→→			CVC N. America
<b>Peptide</b>	NY-ESO-1 + IFA	Ovarian	→→→→→			CVC N. America
	NY-ESO-1 + IFA + CpG	NSCLC	→→→→→			CVC Europe CVC N. America
	Melan-A + IFA + CpG	Melanoma	→→→→→			CVC Europe
	NY-ESO-1/ Tyrosinase/ Melan-A/ MAGE-4/ MAGE-10 + GM-CSF	Melanoma NSCLC	→→→→→			CVC Australasia CVC Europe CVC N. America
<b>Dendritic Cells</b>	Peptides	Melanoma	→→→→→			CVC Europe
	Peptides	Melanoma	→→→			CVC N. America
	NY-ESO-1 + ISCOM	Melanoma	→→→→→			CVC Australasia
<b>Immune Potentiators</b>	CTLA.A4	Sarcoma	→→→			CVC N. America

## Advances

The CVC's novel immunological monitoring strategies now allow the precise assessment and quantification of CD8+ T cell, CD4+ T cell, and antibody responses to the vaccines being investigated. The ability to induce and monitor immunization has allowed the CVC to continue the rational refinement and optimization of cancer vaccines, and vital data on variables such as constitution and delivery have been obtained. The CVC has used these monitoring strategies to show that patients receiving CVC vaccines have been successfully immunized against cancer antigens. In fact, the CVC was the first to show a fully integrated immunological response to a cancer vaccine containing a recombinant protein target.

The CVC's successes in identifying targets and refining vaccines have been recognized by both academia and industry, leading to codevelopment and licensing agreements with companies such as GlaxoSmith-Kline, CSL Ltd, and Therion.

### Participating Investigators:

#### CVC Asia

- Drs. Hiroshi Shiku and Shin-ichi Kageyama, Mie University School of Medicine, Mie, Japan
- Drs. Eichi Nakayama, Yuji Noguchi, Hiromi Kumon, and Hisashi Wada, Okayama University Medical School, Okayama, Japan
- Drs. Yasuhiro Nagata and Matsutoshi Matsuo, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
- Dr. Wei-Feng Chen, Peking University, Beijing, China
- Dr. Yu Wang, Beijing Cancer Hospital, Beijing, China

#### CVC Australasia

- Drs. Jonathan Cebon, Ian Davis, and Weisan Chen, LICR Melbourne Branch for Tumor Biology/Austin Hospital, Melbourne, Australia
- Dr. Rodney Dunbar, The University of Auckland, Auckland, New Zealand

#### CVC Europe

- Drs. Vincenzo Cerundolo and Adrian Harris, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom
- Dr. Elke Jäger, Krankenhaus Nordwest, Frankfurt, Germany
- Drs. Marie Marchand, Nicolas Van Baren, Pierre Coulie, and Thierry Boon, LICR Brussels Branch of Human Cancer Cell Genetics/Clinique Universitaires Saint-Luc, Brussels, Belgium
- Drs. Daniel Speiser, Danielle Lienard, Pedro Romero, Immanuel Luescher, and Jean-Charles Cerottini, LICR Lausanne Branch of Tumor Immunology/Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

## The Next Phase

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The CVC is at a pivotal phase in its clinical development of cancer vaccines. More extensive Phase II trials, which include large numbers of patients, are now required to further investigate and validate the CVC preliminary data that correlate an immune response with a clinical response. The major endpoint of these trials is to measure therapeutic efficacy of cancer vaccines.

Initial indications—although from a Phase I trial with small patient numbers—suggest that at least one of the CVC vaccines may impact upon relapse-free survival in melanoma patients. It is now vital that the CVC conduct pivotal Phase II trials to confirm this observation. CRI and LICR are engaged in a campaign to augment their resources to ensure that this happens.

- Drs. Alexander Knuth, Dirk Jäger, and Alfred Zippelius, University Hospital Zürich, Zürich, Switzerland
- Drs. Michael Pfreundschuh and Christoph Renner, University of Saarland Medical School, Homburg, Germany
- Drs. Djordje Atanackovic and Susanna Hegewisch-Becker, University Hospital Hamburg-Eppendorf, Hamburg, Germany

### CVC North America

- Drs. Charles Hesdorffer, Maha Ayyoub, and Danila Valmori, Columbia-Presbyterian Medical Center, New York, USA
- Drs. Jakob Dupont, Robert Maki, Padmanee Sharma, Dean Bajorin, Sacha Gnjatic, Achim Jungbluth, Gerd Ritter, Harry Herr, and Lloyd Old, LICR New York Branch of Human Tumor Immunology/Memorial Sloan-Kettering Cancer Center, New York, USA
- Dr. Svetomir Markovic, Mayo Clinic, Rochester, USA
- Dr. Anna Ferrari, Mount Sinai School of Medicine, New York, USA
- Drs. Nina Bhardwaj, Sylvia Adams, David O'Neill, and Steven Burakoff, New York University School of Medicine, New York, USA
- Drs. Nasser Altorki and Yao-Tseng Chen, Weill Medical College of Cornell University, New York, USA
- Drs. Kunle Odunsi and Feng Qian, Roswell Park Cancer Institute, Buffalo, USA
- Dr. Craig Slingluff, University of Virginia, Charlottesville, USA
- Drs. John Kirkwood and Hassane Zarour, University of Pittsburgh Medical Center, Pittsburgh, USA

## About LICR

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The Ludwig Institute for Cancer Research engages leading scientists and clinicians from around the world in an integrated effort to understand and control the global problem of cancer. LICR is convinced that early-phase clinical investigations are the last step of the initial discovery phase and not the first step of a new drug development phase. Thus, in addition to an abiding commitment to fundamental laboratory investigation, LICR takes responsibility for identifying and assessing the therapeutic utility of discoveries made in its laboratories by sponsoring and conducting clinical trials.

## About CRI

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The Cancer Research Institute was founded in 1953 to foster research that will yield an understanding of the immune system and its response to cancer, with the ultimate goal of developing immunological methods for the treatment and prevention of the disease. To accomplish these goals, CRI supports scientists at all stages of their careers and funds every step of the research process, from basic laboratory studies to clinical trials testing novel immunotherapies. Guided by a Scientific Advisory Council, which includes four Nobel Prize winners and 24 members of the National Academy of Sciences, CRI awards fellowships and grants to scientists around the world. The Institute's scientific strength and excellence are matched by its fiscal integrity with 90 cents of every dollar raised used to directly support its research and medically related programs.

Lloyd J. Old, M.D., Director, Ludwig Institute for Cancer Research and  
Director, Cancer Vaccine Collaborative

Jill O'Donnell-Tormey, Ph.D., Executive Director, Cancer Research Institute

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**For more information, please contact:**

Cancer Research Institute  
Manager of Communications  
[info@cancerresearch.org](mailto:info@cancerresearch.org)

Ludwig Institute for Cancer Research  
Office of Communications  
[communications@licr.org](mailto:communications@licr.org)



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Cancer Research Institute  
Ludwig Institute for Cancer Research