



# Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



May 15, 1998  
Volume 58 • Number 10  
PP. 2053-2268  
ISSN 0008-5472 • CNREA 8

# InvivoGen

## Tools for Gene Therapy

**Innovative solutions for gene therapy (with an initial focus in cancer) to accelerate the rate of gene therapy research by providing ready to use novel multigenic vectors and optimized kit accessories.**

### Optimized Vectors

- single selection in bacteria and mammalian cells
- native proteins expressed in mammalian cells
- optimized transcription units, e.g. 5' & 3' UTR
- transcriptional pause for decreased interference
- forced expression of gene using IRES
- full CMV promoter including intron IA
- bifunctional fused protein products

### Gene Families

- tumor suppressors, e.g. p53
- suicide genes, e.g. HSV1tk
- gap junctions, e.g. Connexins
- apoptosis, e.g. Bik
- cell cycle regulation, e.g. p27
- immune enhancers, e.g. IL-2
- bound reporter genes, e.g. PLAP
- cellular matrix proteins, e.g. Decorin

### Complete Kit Solutions

- ready-to-use multigenic vectors
- control vectors
- ready-to-use prodrugs
- microwavable media with antibiotic
- transformed *E. coli*
- mycoplasma curing kit
- reporter assay kit

### Vector Development Partnership

- place your gene of interest in our optimized vectors with your choice of associated gene(s)
- 2 weeks for new constructions
- complete kit from your cDNA
- guaranteed undetectable endotoxins (LPS)
- expression in bacteria and mammalian cells
- transfected mammalian cells, e.g. B16

[www.invivogen.com](http://www.invivogen.com)

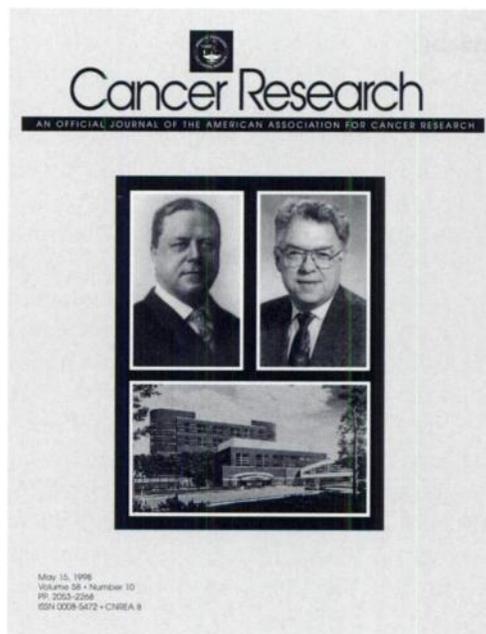
Full documentation of genes and backbones  
(references, sequences, maps and results)  
More than 50 multigenic vector gene combinations  
with more being created weekly

**Toll Free (U.S.) (888) 457-5873**

**Outside U.S. (619) 457-5873**

Register for our mailing list by visiting our web site or by calling our toll free number.  
Receive newsletters, catalogs, and updates.

**3950-A Sorrento Valley Blvd, San Diego, Ca 92121**



Roswell Park Cancer Institute, in Buffalo, New York, celebrates its Centennial in 1998 with a newly constructed and renovated campus (cover), and with a rich heritage of leadership in the worldwide effort to discover the scientific bases for cancer and effective therapies for the many diseases that come under its umbrella. The vision of the Institute all started with Dr. Roswell Park (top left), one of the outstanding surgeons of the late 19th and early 20th centuries.

Dr. Park's passion for establishing the first cancer research laboratory in the world in 1898 was driven by his recognition of the future tragedy that cancer would bring and by his concern over the lack of an organized effort to investigate the nature of cancer and discover ways to improve treatment through multidisciplinary research. This effort, he believed strongly, had to engage all scientific disciplines working in an institutional setting. As Dr. Park stated, "Only by a deliberate, well planned, combined attack from various directions by means fitted for such work could real advances be made, and the relationship of laboratory work, clinical study, and education must be closely associated." This was a revolutionary approach to the investigation of cancer since prior to this, if cancer research was conducted at all, it was conducted in a single disciplinary manner and in an *ad hoc* fashion.

The concept of developing a cancer research laboratory with a grant from the government of New York State again set Dr. Park apart as a pioneer in funding biomedical research, establishing the precedent for the modern day structure of government funding of, and community support for, biomedical research on specific diseases. (The laboratory continued to receive an annual grant appropriation from 1898 to 1911, when it formally became a State institution.) Dr. Park forced the government of New York State to recognize for the first time that cancer was a public health problem that was on the rise

worldwide, and he influenced other states and countries (England, Germany, Russia, France, and Japan) to do the same. Dr. Park believed it was the proper function of government to help with biomedical research in cancer. His multidisciplinary approach to the study of cancer was implemented not only at his namesake institution, but it also became the blueprint for modern day comprehensive cancer centers, particularly those developed since the passage of the National Cancer Act in 1971.

By 1907, the cancer research conducted by Dr. Park and Dr. Harvey R. Gaylord, the second Director of the Institute, stressed that an organism was, in part, involved in the cause of cancer and developed immunological approaches to inhibit the growth of cancer. Meanwhile, Dr. George H. A. Clowes established the first cancer chemotherapy program at the Institute. The research of these three pioneers, along with that of a multidisciplinary senior staff of 15, including the famous biologist Dr. Leo Loeb, who worked on the biology of transplanted tumors, was beginning to have an impact nationally and internationally. The Institute staff collaborated with Professor A. Borrel at the Pasteur Institute, Professor Carl Olaf Jensen of Copenhagen, Madame Curie of the University of Paris, Dr. Peyton Rous of the Rockefeller Institute (who was familiar with the work of Dr. Gaylord and colleagues on the parasitic theory of cancer), Professor Von Leyden, Head of the German Society of Cancer Investigation, Professor Ludwig Aschoff of Freiburg, Dr. Morau in France, Dr. Ehrlich in Frankfurt, and Dr. Bashford in London. Within a few years of its founding, the Institute received worldwide commendation and encouragement. Sir William Osler, who was a frequent visitor to the Institute, said he was "delightfully impressed on [his] recent visit with the character of research going on."

Drs. Park, Gaylord, and Clowes and other senior staff members enthusiastically added their influence to that of those interested in establishing the American Association for Cancer Research (AACR) as a national forum in which to share and exchange cancer research findings and concepts. Drs. Gaylord and Clowes, charter members of the AACR, participated in organizational meetings on May 7–8, 1907, and hosted the first national AACR meeting in Buffalo in 1908. Roswell Park Cancer Institute also hosted national meetings of the AACR on April 11, 1911, and April 17, 1924, and a number of senior staff members have been officers of the AACR: Dr. Harvey R. Gaylord (Secretary, 1907–09; President, 1909–10, 1916–17; Vice President, 1910–11); Dr. Leo Loeb (President, 1911–12); Dr. Gary N. Calkins (President, 1913–14); Dr. Burton T. Simpson (President, 1926–27, 1940–41); Mr. Millard C. Marsh (Vice President, 1933–34; President, 1934–35; Secretary-Treasurer, 1935–36); Dr. Alphonse A. Thibaudeau (Secretary-Treasurer, 1936–42; Vice President, 1942–45); Dr. George H. A. Clowes (Vice President, 1937–38, President, 1938–39); Dr. Jacob Furth (President, 1957–58); Dr. Theodore S. Hauschka (Vice President, 1958–59, President, 1959–60); Dr. James F. Holland (President, 1970–71); and Dr. Enrico Mihich (President, 1987–88).

At the 1908 AACR meeting hosted in Buffalo, Dr. Gaylord was authorized to submit an AACR resolution to President William H. Taft, proposing an appropriation for cancer research and the creation of a Department of Cancer Research within a Bureau of Public Health. President Taft was impressed and stated, "A close investigation into the subject of cancer may give us light upon this dreadful human scourge." President Taft then visited Roswell Park Cancer Institute on April 30, 1910, to enthusiastically support the resolution. This first attempt at a national cancer program was defeated in the 61st Congress. However, this part of Dr. Park's dream was realized later when President Franklin D. Roosevelt and subsequently President Richard M. Nixon made research on the problem of cancer a national priority. President Roosevelt, who had visited the Institute as Governor of New York and was familiar with the cancer problem in the state and the activities at the Institute, saw from this exposure the benefit of a national cancer program, and as President, he signed the National Cancer Institute Act in 1937. President Nixon signed the National Cancer Act in 1971, after much debate in Congress, including a Congressional subcommittee hearing held at Roswell Park on October 11, 1971.

One hundred years after the start of Dr. Roswell Park's noble experiment and revolutionary model for studying cancer in a multidisciplinary manner in an institutional setting, many investigators, including Roswell Park staff members, have contributed to our better understanding of cancer and to national and international associations such as the AACR, the Association of American Cancer Institutes, the International Union Against Cancer (UICC), the American Cancer Society, the American College of Surgeons, and others.

Each administration at Roswell Park Cancer Institute has contributed notably to Dr. Park's philosophy of how to conduct cancer research and carry out the mission of the Institute. Dr. Gaylord's administration (1904–1924) was highlighted by the Institute formally becoming a New York State institution in 1911, by studies on the parasitic theory of cancer, the immunity of cancer, and cancer chemotherapy, by the construction of the first 30-bed hospital devoted to treating cancer, and by the acquisition of an experimental farm. Dr. Gaylord also recruited Nobel Laureates Drs. Carl and Gerty Cori to the Institute, where they did much of their carbohydrate metabolism research. Dr. Burton T. Simpson (1924–1943) emphasized clinical activities, saw the construction of a 78-bed hospital, expanded facilities for radiation therapy, developed a free statewide pathological diagnostic service for any physician or dentist, and negotiated with New York State to place the Institute within the New York State Department of Health in 1926. Dr. Louis C. Kress (1945–1952) crafted an intensive educational program that included public education and training for medical students and physicians, and he initiated post-

war plans with Governor Thomas Dewey to expand treatment, research, and educational facilities at the Institute. Upon the sudden death of Dr. Kress, it was left to Dr. George E. Moore's remarkable and outstanding stewardship (1953–1967) to develop a master plan that led to unprecedented expansion of staff and of clinical and research facilities and programs, the formation of a nonprofit corporation to receive and administer research grants and gifts, and the establishment of the Roswell Park Graduate Division of the State University of New York at Buffalo. When Dr. Moore stepped down as Director, Dr. James T. Grace, Jr. (1967–1970) continued to implement Dr. Moore's plans, reorganized the Institute into distinct administrative areas of scientific affairs, clinical affairs, and education, and initiated an Institute program for the study of viral carcinogenesis. The unfortunate car accident that claimed the lives of Dr. and Mrs. Grace left the further development of the Institute to Dr. Gerald P. Murphy (1970–1985). Dr. Murphy was responsible for inviting Representative Paul G. Rogers of the U. S. House of Representatives to Roswell Park to hold a hearing of his Congressional subcommittee on the proposed National Cancer Act in 1971, and he was appointed to the first National Cancer Advisory Board in 1972. His administration was marked by the expansion of programs and clinical and research facilities. He promoted many clinical research studies using various cooperative groups and was chairman of the extramural Organ Site Program sponsored by the National Cancer Institute. Dr. Murphy also became Secretary-General of the UICC in 1974, a position he still holds today. Dr. Thomas B. Tomasi (1986–1996), first President and CEO of the Institute, was appointed to continue the revitalization and expansion of scientific and clinical programs, recruit new staff, and enhance patient care. This noted immunologist also helped forge a new partnership with New York State and the community, which led to New York State contributing \$303 million to the Major Modernization Project scheduled for completion during the Centennial celebration.

Dr. David C. Hohn (*top right*) was appointed current President and CEO in February 1997. Like other directors of modern day cancer centers, he will face the most daunting challenge to date. Dr. Hohn must lead Roswell Park Cancer Institute into the 21st Century with new approaches in governance as on October 15, 1998, the Institute will end its association with the New York State Department of Health and become a Public Benefit Corporation. This new structure of governance will enable the Institute to survive and thrive in a competitive health care environment, while preserving the same commitment to cancer research, treatment, and education with which Dr. Roswell Park led his fledgling multidisciplinary cancer laboratory into the 20th Century.

Edwin A. Mirand