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Cellular and Molecular Targets of Cancer Therapy

Forty-second Annual Symposium on Fundamental Cancer Research

October 24 - 27, 1989

Stouffer Greenway Plaza Hotel • Houston, Texas

The symposium highlights the most exciting research related to targets for cancer therapy. The program covers the progress being made in those areas of biology related to the regulatory processes of cell growth and mechanisms of cytotoxicity. Each session deals with a specific cellular or tumor compartment as a potential target of therapy. These include targets located in the plasma membrane, the cytoplasm, the nucleus, and non-malignant targets which include the immune system, extracellular matrix, and viruses.

Ernst W. Bertner Award and Memorial Lecture - Gertrude Elion, Wellcome Research Laboratories
Keynote Address - Ira Pastan, National Cancer Institute
Special Lecture - Robert A. Weinberg, Massachusetts Institute of Technology

Additional speakers will include:

Robert M. Bell, Duke
Vilhelm A. Bohr, NCI
Donald S. Coffey, Johns Hopkins
Jack S. Cohen, NCI
O. Michael Colvin, Johns Hopkins
Thomas Curran, Roche Institute
Leonard C. Erickson, Loyola
Isaiah J. Fidler, M. D. Anderson
Gordon Gill, UC at San Diego
William A. Haseltine, Dana-Farber
Susan B. Horwitz, Albert Einstein
Laurence Hurley, University of Texas
Mark A. Israel, NCI
Adi Kimchi, Weizmann Institute
Stephen J. Lippard, MIT
Marc E. Lippman, Georgetown University
Frank McCormick, Cetus Corporation
Garth L. Nicolson, M.D. Anderson
Anita Roberts, NCI
Warren E. Ross, University of Louisville
Daniel V. Santi, UC at San Francisco
Thomas A. Waldmann, NCI

Symposium Cochairmen: William Plunkett, Ph.D. • William A. Brock, Ph.D.

Call for Posters: Abstracts are requested for the 1989 Research Symposium poster session(s). Abstracts not exceeding one page, should be typed double-spaced on plain, 8.5 by 11 inch paper and must be received no later than August 15, 1989. Participants will be notified of their posters' acceptance by mail. Submit abstracts to: Anthony J. Mastromarino, Ph.D., Office of the Vice President for Research - Box 101, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030.

For additional information, please contact Pam Evans, Conference Services-HMB 131, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030. Phone: (713) 792-2222.

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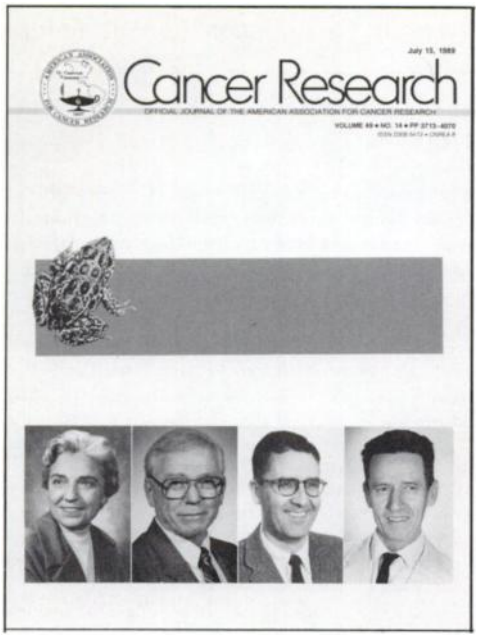

In these times, when cloning of early cleavage nuclei in mammals is becoming commonplace, it is instructive to consider when and by whom the cloning of multicellular organisms was first successfully performed. In 1952, Robert Briggs and Thomas J. King, at that time members of the Institute for Cancer Research in Philadelphia, developed the procedure for nuclear transplantation in the northern leopard frog, *Rana pipiens.* They obtained normal development of tadpoles by the insertion of single nuclei from undifferentiated blastula cells into enucleated eggs (R. Briggs and T. J. King. Proc. Natl. Acad. Sci. USA, *38:* 455–463, 1952). This landmark study demonstrated the multipotentiality of the undifferentiated nucleus, and subsequent studies yielded fertile adult frogs, demonstrating totipotentiality (R. G. McKinnell, J. Hered. *53:* 199–207, 1962). Extension of these studies by others to different amphibian species, to the insect *Drosophila*, and to the teleost fish reveal their undifferentiated blastula nuclei to be totipotent. Recently, even the early cleavage nuclei of mammals were shown to be totipotent. For their prototype experiments, Briggs and King, in 1972, were awarded the Leopold Mayer Prize of the Academie des Sciences; they were the first Americans to receive this highest award of the French Academy.

A striking sequel, of special relevance to perceptions of cancer development, was the finding by King and McKinnell (reported in *Cell Physiology of Neoplasia,* pp. 591–617. Austin, TX: University of Texas Press, 1960), King and DiBerardino (Ann. NY Acad. Sci., *126:* 115–126, 1965), and McKinnell *et al.* [Science (Wash. DC), *165:* 394–396, 1969] that normal development to the tadpole stage occurred from transplantation of nuclei of the herpes virus-induced frog tumor, Lucké renal adenocarcinoma, into enucleated eggs. The precision of orchestration of gene activation and regulation sufficient to create a viable functioning multicellular organism is thus retained throughout the neoplastic transformation!

The current challenge is to clone successfully nuclei of differentiated adult cells. The production of feeding tadpoles from adult erythroycte nuclei that advance one-third of the way to metamorphosis attests to the near totipotency of nuclei of terminally differentiated cells (M. DiBerardino, N. Orr, and R. McKinnell. Proc. Natl. Acad. Sci. USA, *83:* 8231–8234, 1986). The activation of nearly the entire genome of erythrocyte nuclei suggests that even the genome of adult cancer cells might be induced to undergo more extensive activation.

A history of nuclear transplantation and its significance and a complete bibliography to 1985 are available (R. McKinnell. *Cloning of Frogs, Mice and Other Animals.* Minneapolis, MN: University of Minnesota Press, 1985; R. G. McKinnell. *Cloning: Nuclear Transplantation in Amphibia.* Minneapolis, MN: University of Minnesota Press, 1978). DiBerardino is the author of a recent review (Am. Zool., *27:* 623–644, 1987).

Marie A. DiBerardino, *left*, is Professor of Physiology at the Medical College of Pennsylvania, and Robert G. McKinnell, *second from left*, is Professor of Genetics and Cell Biology at the University of Minnesota. Initially, DiBerardino was associated with Briggs; later, both were associated with King in Philadelphia and are continuing their studies in nuclear transplantation. Thomas J. King, *second from right*, is Deputy Director, Lombardi Cancer Research Center, Georgetown University Medical Center, Washington, DC and is Treasurer of the AACR. Robert Briggs, *right*, died in 1983 after serving for many years as Research Professor and subsequently Chairman, Biology Department, Indiana University, Bloomington. The frog was produced by transplanting a nucleus from a kandiyohi mutant frog into the cytoplasm of an enucleated egg obtained from a wild-type female. The mottled mutant skin pigment pattern of the cloned frog provided unequivocal evidence that the frog resulted from genetic instructions of the transplanted nucleus, not the enucleated egg (from McKinnell, 1962).

We are indebted to Dr. McKinnell for the photographs and help in preparing the legend. Photographs of Briggs and King, made in 1960, were obtained courtesy of the Institute for Cancer Research.

Sidney Weinhouse