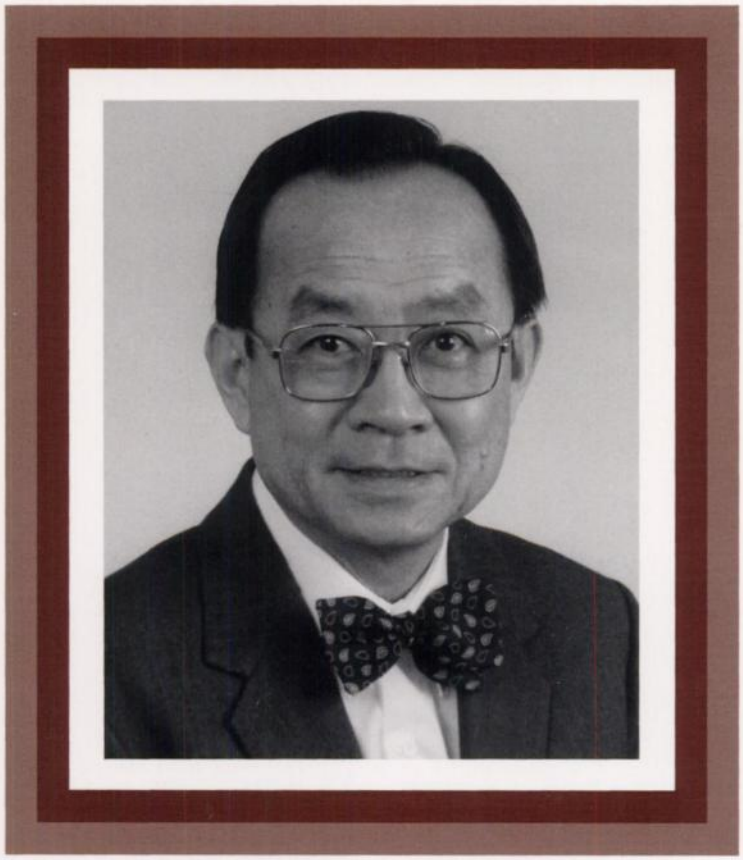
Cancer Research

AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH



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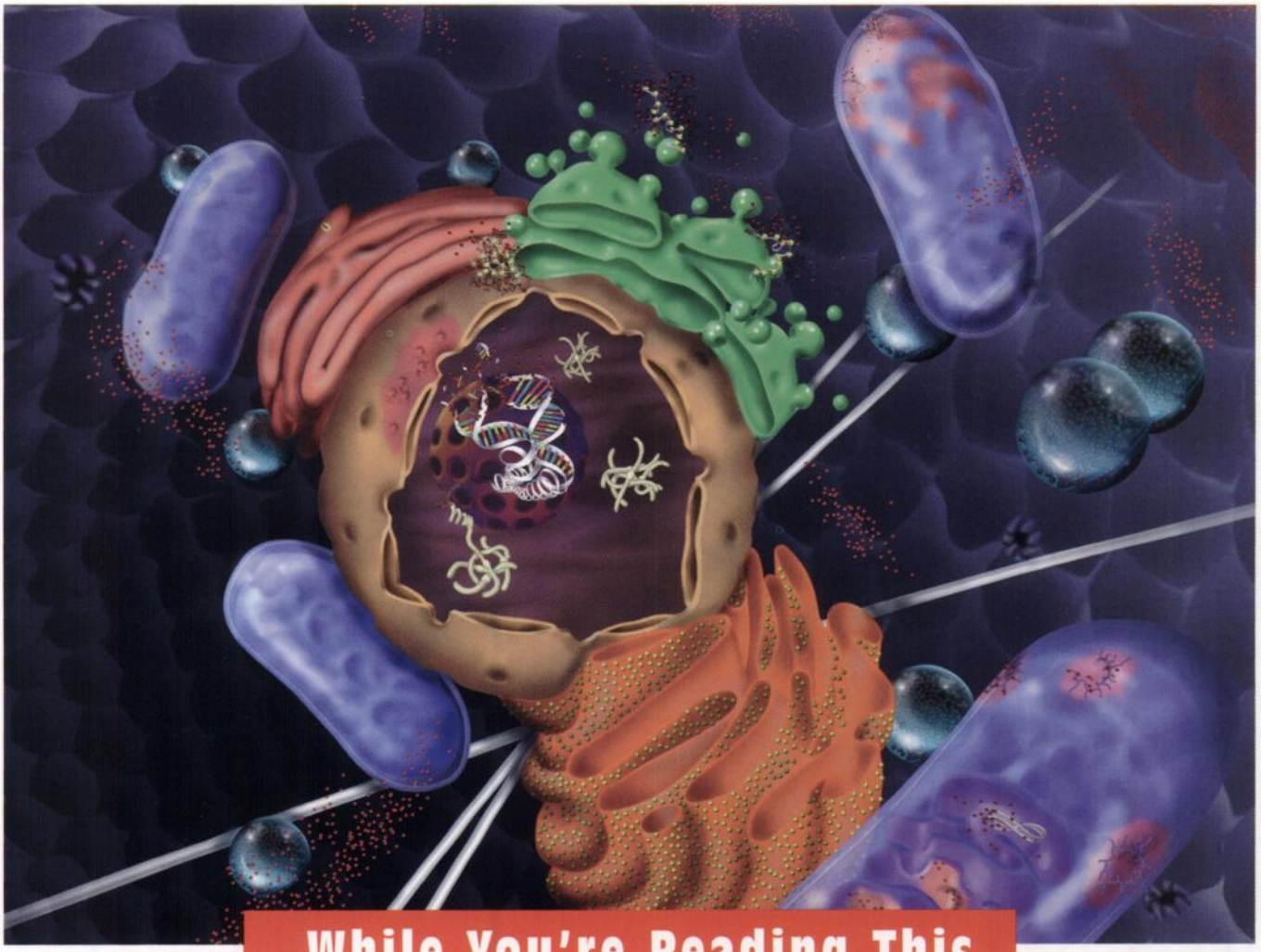

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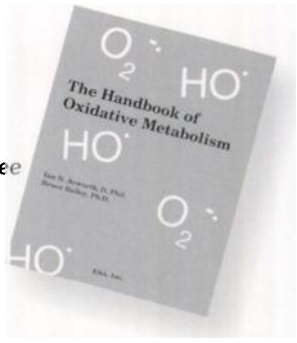

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SESSION TOPICS

Lectures

- Rational Drug Targets
- Pitfalls of Clinical Trials
- Principles of Study Design
- Biostatistics for the Clinical Trialist
- Preclinical Pharmacology
- Phases I, II, and III Trial Design
- Principles of Clinical Pharmacology and Pharmacokinetics
- Excellent Laboratory Correlates in Early Phase Clinical Trials
- Regulatory and Ethical Issues
- Special Considerations for Prevention Trials
- Implications of Molecular Epidemiology Research

Small Group Discussions

- New Measures of Outcome
- Cytostatic Agents, Angiogenesis Inhibitors, Growth Factors
- Clinical Trials with Biologics
- Research Abstract Presentations that Audiences Remember
- Special Considerations for Surgical Oncology Trials
- The Challenge of Combined Modality Trials
- Special Considerations for Pediatric Oncology Trials
- Special Considerations for Radiation Oncology Trials
- Visiting with the Patient: Presentation of a Clinical Trial

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DEVELOPMENTAL BIOLOGY AND CANCER

June 9-10, 1998
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Bethesda, Maryland

June 9

Overview: Developmental Biology and Cancer
Mario R. Capecchi, Ph.D.

Session 1: PAX Genes
Moderator : Phillip A. Sharp, Ph.D.
PAX Genes in Development
Peter Gruss, Ph.D.
The Role of Chimeric Paired Box Transcription Factors in the Pathogenesis of Pediatric Rhabdomyosarcoma
Frederic G. Barr, M.D., Ph.D.
PAX Genes in B Cell Development and Disease
Meinrad Busslinger, Ph.D.

Session 2: Embryonal Tumors
Moderator: Sharon B. Murphy, M.D.
Id Gene Expression as a Key Mediator of Tumor Cell Biology
Mark A. Israel, M.D.
Developmental Basis of Retinal-Specific Induction of Cancer by RB1 Mutation
Brenda L. Gallie, M.D.
RET: Developmental and Tumor Syndromes
Bruce A. J. Ponder, Ph.D.

Session 3: Embryonal Tumors and Breast Cancer
Moderator: Ray L. White, Ph.D.
Genomic Imprinting and Cancer
Andrew P. Feinberg, M.D.
Multiple Roles for the Wilms' Tumor Suppressor, WT1
Nicholas D. Hastie, Ph.D., B.Sc.
Functional Analysis of the BRCA1 Gene Product
David Livingston, M.D.
Reversion of the Malignant Phenotype in Human Breast Cancer Epithelial Cells: Structure is the Message
Mina J. Bissell, Ph.D.
Mammary Gland Development and Carcinogenesis: Molecules at the Crossroads
Lewis A. Chodosh, M.D., Ph.D.

June 10

Session 4-A : Leukemia and Developmental Genes
Moderator: Louise C. Strong, M.D.
Identification and Characterization of Collaborating Oncogenes in Lymphomagenesis
Anton Berns, Ph.D.
BCL-2 Family Death Regulators in Development and Homeostasis
Stanley J. Korsmeyer, M.D.
***ALL-1* and *TCL1* Role in Human Leukemias and Mammalian Development**
Carlo M. Croce, M.D.

Session 4-B: Leukemia and Developmental Genes: Functional Genes
Moderator: Günter Schütz, M.D.
Intersections Between Blood Cell Development and Leukemia Genes
Stuart H. Orkin, M.D.
CBF: A Central Player in Hematopoiesis and Leukemia
Nancy A. Speck, Ph.D.
Chromosomal Translocations and What They Do in Leukemias
Terry H. Rabbits, Ph.D., F.R.S.

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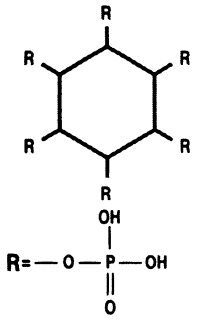
IP6



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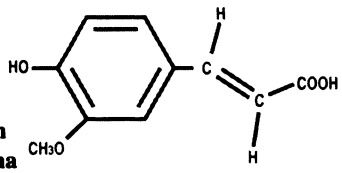

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Dr. T. Otake, Osaka Pref. Institute of Public Health

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Dr. H. Sugano, Japanese Foundation for Cancer Research
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Applicants are encouraged to submit abstracts for poster presentation.

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COVER LEGEND

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This issue we feature T. Ming Chu, an early pioneer in using tumor cell products for the diagnosis and therapy of cancer, who played a leading role in the discovery of prostate specific antigen (PSA) and the development of the PSA test. Dr. Chu is Chair of Diagnostic Immunology Research at Roswell Park Cancer Institute. A native of Taiwan, he received a Ph.D. in Biochemistry from Pennsylvania State University in 1967. After spending 3 years at the Medical Foundation of Buffalo and Buffalo General Hospital, he joined Roswell Park. Shortly after joining the Institute, with the support of the State of New York and the National Cancer Institute/National Institutes of Health, Dr. Chu embarked upon a major prostate cancer research project with a team of able colleagues. His goal was to identify prostate tumor-specific or associated antigens, and to develop a blood test for early detection of prostate cancer.

Dr. Chu's work, in collaboration with Ming C. Wang, eventually resulted in the discovery and purification of PSA from the prostate (Invest. Urol., *17*: 159, 1979). With PSA and antiPSA in hand, he turned his attention to the development of the PSA test. Working with Lawrence D. Papsidero, he was able to demonstrate the presence of PSA in the sera of prostate cancer patients (Cancer Res., *40*: 2428, 1980). Noteworthy then, and more so now, was the observation that circulating PSA exhibits predominantly as 100 kDa versus that of prostate tissue as 33 kDa, and it is "'contaminated'' with normal serum protein. This is also the first report describing the existence of complexed PSA versus free PSA as it is called today.

Together with Manabu Kuriyama, Dr. Chu then developed an enzyme linked immunosorbent assay for PSA (Cancer Res., *40*: 4658, 1980). The results revealed the potential diagnostic value of PSA. In patients with benign prostatic hypertrophy, PSA levels were greater than those of healthy controls. Patients with prostate cancer demonstrated even higher PSA levels, which increased with increasing disease stage. Working together with the National Prostatic Cancer Project urologists, he and Gerald P. Murphy evaluated the additional clinical value of PSA (Cancer Res., *41*: 3874, 1981). PSA was of prognostic value in patients with advanced disease. Serial PSAs were also of value in monitoring prostate cancer patients undergoing treatment. Significantly, patients with localized prostate cancer, who underwent curative therapy and later developed metastasis, were found to exhibit increasingly elevated PSA before disease recurrence was detected clinically. Furthermore, Dr. Chu and his laboratory colleagues showed that PSA is expressed *in vitro* and *in vivo* by prostate tumors and is a marker for prostate epithelial cells (J. Natl. Cancer Inst., *66*: 37, 1981 and *68*: 99, 1982). Hence, the basis for the use of PSA in the diagnosis of prostate cancer was established firmly.

Dr. Chu also reported the first experiments characterizing fundamental properties of PSA. Together with Drs. Wang and Rueyming Loor, he showed that PSA biochemically is a glycoprotein in isomeric forms (*Methods in Cancer Research*, Vol. 19, p. 179, New York: Academic Press, 1982; Int. Res. Commun. System Med. Res., *11*: 327, 1983). He then tried to discern what its biological function is, if any. Together with Yoshihito Ban, he presented the answer in a ground-breaking paper, which is the first report that PSA biologically is a unique protease (Biochem. Biophys. Res. Commun., *23*: 482, 1984). This finding also provided the genesis of today's "PSA-protease inhibitor" complexes.

A simplified purification procedure for PSA and the preparation of antiPSA monoclonal antibody further facilitated the widespread use of the PSA test. (Oncology, *39*: 1, 1982; Hybridoma, *2*: 139, 1983; J. Urol., *141*: 152, 1989). Dr. Chu is also responsible for the transfer of PSA technology to the biomedical industry, which subsequently has made PSA reagents readily available. Consequently, expanded basic research and clinical application of PSA was extensively conducted by investigators all around the world. One measure of the profound impact of Dr. Chu's pioneering PSA work can be quantified from the exponential increase in the number of papers published on PSA from only one in 1979 to the rate of more than one a day at present. The tremendous number of investigations on PSA eventually led to the approval of the PSA test by the Food and Drug Administration for the purpose of monitoring in 1986 and for diagnosis of prostate cancer in 1994.

Dr. Chu made a seminal discovery and then pursued its translational research with global impact on prostate cancer patient care (Tumor Biol., *18*: 123, 1997). In addition to PSA, his research interests include immunodiagnosis of breast cancer, immunohistochemistry of ductal carcinomas, experimental cancer immunotherapy, and activation of TGF-β. He has published over 300 research articles and holds 11 patents related to diagnosis and therapy of cancer. He has been a member of the American Association for Cancer Research since 1973. Dr. Chu has received numerous awards, including the Presidential Award of the American Urological Association, the Dornier Innovative Research Award of the American Foundation for Urologic Disease, as well as the Abbott Award of the International Society for Oncodevelopmental Biology and Medicine, the Schoellkopf Medal of the American Chemical Society, and the Van Slyke Award of the American Association for Clinical Chemistry. He is also a recipient of the Distinguished Alumnus Award from both Pennsylvania State University and North Carolina State University.

Sidney Weinhouse