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The Pezcoller Foundation, Trento, Italy

The Pezcoller Foundation is a non-profit organization created in 1979 by Prof. Alessio Pezcoller, who was the chief Surgeon of the S. Chiara Hospital of Trento, Italy. The Foundation, among its activities, annually sponsors a symposium at the cutting edge of basic research. These symposia are structured to favor discussions among participants.

Ninth Pezcoller Symposium, June 4-7, 1997, Rovereto, Italy: The Biology of Tumors

Co-Chairs: E. Mihich and C. Croce; Program Committee: E. Mihich (Chairman), C. Croce, J. Allison, T. Boon, G. Draetta, D. Hanahan, R. Jain and D. Livingston

June 4, AM, Session I: The Genetics of Tumor Heterogeneity, Co-Chairs: G. Draetta and M. Pierotti

Ronald DePinho Role of INK^{4A} in the development of normal and neoplastic cells
Anton Berns Identification and characterization of collaborating oncogenes in compound mutant mice

June 4, PM, Session II: The Genetics of Tumor Heterogeneity and Tumor Differentiation, Co-Chairs:

P.G. Pelicci and F.J. Rauscher, III

David Ward Allele discrimination using a rolling circle amplification technology
Joe Gray Genetic selection during tumor evolution

Douglas Hanahan Cellular and molecular parameters of pathways to cancer

June 5, AM, Session III: New Method to Measure Differentially Genes and Gene Products, Co-Chairs: R. White and K. Helin

Thomas Gingeras High density oligonucleotides arrays platform for genotypic and expression profiling

Paul Meltzer cDNA microarray analysis of gene expression in cancer

Paolo Di Fiore Novel protein: Protein interaction domain

June 5, PM, Session IV: Cell-Cell Interactions and Cell Regulation, Co-Chairs: D. Livingston and P. Comoglio

Rob Michalides Mechanism of growth advantage by overexpression of cyclin D1

John Reed Dysregulation of apoptosis in cancer: Mechanism of Bcl-2 family protein function

Richard Klausner The VHL tumor suppressor gene pathway

June 6, AM, Session V: Tumor Recognition by the Immune System, Co-Chairs: T. Boon and L. Moretta

Pierre Coulie Antigens recognized on human tumors by T lymphocytes

Michael Pfreundschuh Serological analysis of human tumor antigens

Pamela Ohashi Induction of tumor immunity *in vivo*; transient tumor regression in the absence of autoimmunity

James Allison T-cell co-stimulatory approaches to tumor immunotherapy

June 6, PM, Session VI: Tumor Recognition by the Immune System, Co-Chairs: R. Bankert and G. Parmiani

Guido Forni Cytokines and tumor immunogenicity: Towards appropriate cancer vaccines

Cornelis Melief T-cell immunity against cancer, a delicate balancing act

Sharon Evans Leukocyte endothelial cell adhesion in tumor immunity

June 7, AM, Session VII: Tumor Vascularization, Co-Chairs: N. Ferrara and J. Azizkhan

Peter Carmeliet Blood vessel formation in mutant vascular endothelial growth factor (VEGF) and placenta growth factor (PlGF) mice

Georg Brier The role of VEGF in tumor angiogenesis

Rakesh Jain Tumor microcirculation

Carlo Croce Concluding Remarks

For further information, please contact Dr. E. Mihich, Roswell Park Cancer Institute, Buffalo, NY 14263, USA, Tel: 716-845-8225; Fax: 716-845-4542; Email: toscani@sc3103.med.buffalo.edu. For local arrangements, Mr. Giorgio Pederzoli, The Pezcoller Foundation, 38100 Trento, Italy, Tel: 39-461-980 250; Fax: 39-461-980 350. This year, 8 non-invited communications will be accepted on a competitive basis. Please send a 1-page abstract and a letter of endorsement by a senior colleague to Dr. Mihich by May 10, 1997.

THE AMERICAN ASSOCIATION FOR CANCER RESEARCH PRESENTS

***Three Outstanding Training Opportunities
Supported by Major Grants from the National Cancer Institute
Primarily for Postdoctoral and Oncology Fellows***

Waiver of Registration Fees and Partial Subsidy of Lodging and Subsistence Expenses for Qualified Fellows

Molecular Biology in Clinical Oncology

A thorough overview of concepts in molecular biology designed for clinical oncologists in training

June 27-July 3, 1997, The Given Biomedical Institute, Aspen, CO
Stephen H. Friend, L. Michael Glodé, and Jennifer A. Pietenpol, Organizers

- Lectures by leading experts on molecular biology concepts and the latest developments in molecular oncology
 - Small group laboratory sessions to demonstrate the important experimental techniques utilized in molecular biology
 - Career development session and scheduled networking opportunities
 - Application Deadline: March 31, 1997
-

Molecular Biology and Pathology of Neoplasia

(formerly entitled Histopathobiology of Neoplasia)

The Edward A. Smuckler Memorial Workshop

Intensive training in the molecular biology and morphology of human cancer for graduate students and postdoctoral fellows contemplating careers in basic cancer research

July 6-13, 1997, Keystone Resort, Keystone, CO
Robert Low, Course Director

- Twenty-eight hours of hands-on laboratory exercises directed by distinguished pathologists
 - An outstanding series of lectures on rapidly developing areas of cancer research by laboratory directors and other prominent investigators
 - Poster presentations by students and faculty to facilitate further scientific exchange
 - Application Deadline: April 30, 1997
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Methods in Clinical Cancer Research

Co-Sponsored by the American Society of Clinical Oncology (ASCO)

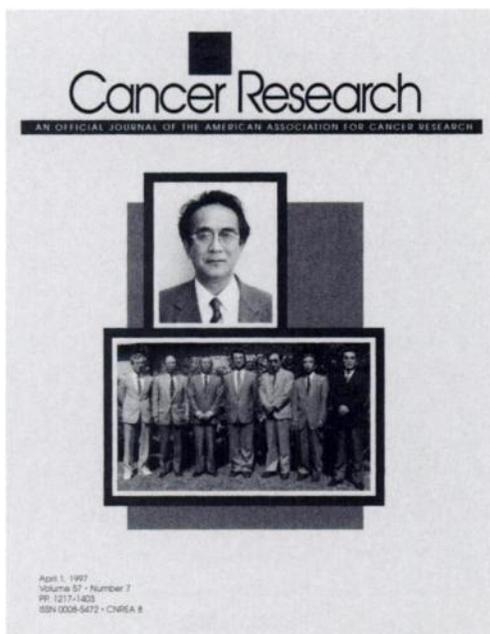
The essentials of clinical trials design for researchers at the level of fellow or junior faculty

July 26-August 1, 1997, Vail Cascade Resort and Club, Vail, CO
Daniel D. Von Hoff and Charles A. Coltman, Jr., Chairpersons

- A series of lectures by leaders in the field covering all elements of clinical trials design
 - Small group discussion sessions on important techniques in clinical research
 - Development of a clinical trial protocol by all participants with detailed critiques by faculty members
 - Category I CME credits through ASCO
 - Application Deadline: April 21, 1997
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Further Information and Application Forms Available from

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The Biological Safety Research Center (BSRC) of Tokyo, Japan, is the organization within the Japanese National Institute of Health Sciences (NIHS) that is responsible for overall safety/risk assessment. From its very early stages, the BSRC has had as its mission the analysis and quality inspection of imported drugs and of chemicals in foodstuffs and drinking water, followed by research on the manufacturing of essential drugs.

In the 1960s, as a consequence of well-publicized toxic effects by chemicals introduced into the human environment, such as thalidomide, arsenic, methyl mercury, and PCB, the public began to express concern over the safety of various chemicals. The BSRC was established in 1978 as an organization to conduct biological studies on the safety and risk assessment of chemicals, such as pharmaceuticals, cosmetics, food, food additives, pesticides, and industrial or household chemicals. The BSRC has a close working relationship with the Pharmaceutical Affairs Bureau and the Environmental Health Bureau of the Ministry of Health and Welfare (MHW). The BSRC presently consists of five divisions staffed by 57 researchers who have multidisciplinary backgrounds in the medical, veterinary, chemical, pharmaceutical, agricultural, and biological fields. The rest of the staff consists of approximately 50 visiting scientists, postgraduate fellows, students, and technicians. The BSRC staff has contributed to projects of international organizations, such as the IARC, WHO, and FAO, and also to the International Conference on the Harmonization of Pharmaceuticals. In addition, GLP inspections on pharmaceuticals and industrial chemicals have been conducted by the senior staff.

The United States National Institute of Environmental Health Sciences (NIEHS) and the BSRC have had a very close relationship since 1981 in keeping with the U.S.-Japan Agreement on Cooperation in Research and Development in Science and Technology. The project entitled "Toxicology" has been established so that these two agencies can exchange information concerning the risk assessment of environmental chemicals.

Pictured on the cover are the immediate past Director of the BSRC, Yuzo Hayashi (*top photo*), and the members of the Senior Board (*bottom photo*). Along with the present Director Yuji Kurokawa (*third from left*) are the Directors of the five Divisions of the BSRC (*from left to right*, exclusive of Dr. Kurokawa): Yasuo Ohno (Pharmacology), Michihito Takahashi (Pathology); Toshio Sofuni (Genetics & Mutagenesis); Tohru Inoue (Toxicology); and Masahiro Nakadate (Risk Assessment); Satoru Tanaka, Chief of the Experimental Animal Care Section, is on the far right.

The study of cancer research was begun at the BSRC by the late Shigeyoshi Odashima, the first Director of the Division of Pathology. His research was divided into two main fields, experimental chemical carcinogenesis and the carcinogenicity testing of environmental chemicals. Bioassays of *N*-nitroso compounds in rats conducted by Akihiko Maekawa (current Director of the Pathology Department, Sasaki Institute, Tokyo) greatly contributed to the establishment of organ-specific carcinogenesis (*J. Cancer Res. Clin. Oncol.*, 109: 178, 1985), of transplacental carcinogenesis (*Gann*, 71: 811, 1980), and of rat neuro-oncogenesis (*Crit. Rev. Toxicol.*, 20: 287, 1990). Dr. Takahashi

and colleagues have investigated rat glandular stomach carcinogenesis using MNG and sodium chloride (*Gann*, 75: 494, 1984; *Carcinogenesis*, 15: 1429, 1994) and hamster pancreatic carcinogenesis using *N*-nitroso compounds (*Carcinogenesis*, 11: 393, 1990). Later, they studied the modifying factors (promoting and inhibitory) based on their own two-stage models of stomach and pancreatic carcinogenesis (*Carcinogenesis*, 13: 1155, 1992; *Carcinogenesis*, 13: 2133, 1992). At present, cell proliferating activity of the modifying factors is being analyzed extensively to elucidate the mechanisms (*Cancer Lett.*, 83: 43, 1994; *Food Chem. Toxicol.*, 33: 21, 1995). Also, mechanistic studies now use transgenic and knockout mice (*Carcinogenesis*, 17: 2455, 1996).

Carcinogenicity tests have been conducted by the BSRC under the auspices of the MHW. The chemicals tested were those with apparent mutagenicity or those structurally related to known carcinogens. Dr. Nakadate, a chemist, had an important role in the selection process. Bioassays included sodium nitrate, sodium nitrite, hydrogen peroxide, caramel, piperonyl butoxide, BHA, and other compounds. The results of these studies, summarized in the Annual Reports of Cancer Research published in Japanese by the MHW, have contributed greatly to the regulatory risk assessment and risk management programs of various agencies. Dr. Maekawa's program on histopathological classification of spontaneous tumors in rats derived from these carcinogenicity tests (*Gann*, 74: 365, 1983). Dr. Kurokawa found that potassium bromate, a food additive, is a novel renal carcinogen in rats (*Environ. Health Perspect.*, 87: 309, 1990). Potassium bromate is an oxidizing agent, and Dr. Kurokawa studied the mechanisms of its oxidative DNA damage *in vivo* using 8-hydroxydeoxyguanosine as a marker not only of potassium bromate but also of nongenotoxic carcinogens (*Cancer Lett.*, 91: 139, 1995).

Carcinogenicity tests have been conducted in the Division of Toxicology, especially on food additives. The late Yoshio Ikeda, the former Director of the BSRC and the first Director of the Division of Toxicology, reported on the induction of forestomach tumors in mice fed furylfuramide (AF-2), a widely used food additive (*Bull. Natl. Inst. Hyg. Sci.*, 100: 80, 1982). The finding led to its ban and had a strong impact on the public, as well as the government; it became the trigger to establish the carcinogenicity of many environmental chemicals in Japan. Another noteworthy study was on the species difference of BHA carcinogenicity using dogs. This was performed by Masuo Tobe, the former Director of the BSRC and the second Director of the Division of Toxicology (*Food Chem. Toxicol.*, 24: 1233, 1986). The work of Tohru Inoue, the present Director of the Division of Toxicology, covers hemopoietic stem-cell toxicology in radiation (*Proc. Natl. Acad. Sci., USA*, 90: 4354, 1993) and chemicals (*Toxicol. Appl. Pharmacol.*, 75: 358, 1984). Dr. Inoue is one of the pioneers who developed the concept of "leukemic stem-cells" (*Int. J. Cell Cloning*, 9: 24, 1991), and now he is establishing a variety of transgenic and knockout mice for use in carcinogenicity and toxicology studies.

The Division of Genetics and Mutagenesis was formerly headed by Motoi Ishidate, Jr., who is known for the development of chromosome aberration tests, using Chinese hamster cells *in vitro* as a screening for chemical carcinogens (*Mutat. Res.*, 48: 337, 1974). Dr. Sofuni and colleagues studied the kinetics of micronucleus formation in relation to chromosomal aberration in mouse bone marrow (*Mutat. Res.*, 127: 129, 1984) and established new sensitive derivatives of *Salmonella typhimurium* tester strain for detection of mutagenic nitroarenes and aromatic amines (*Mutat. Res.*, 234: 337, 1990). Currently they are focusing on *in vivo* gene mutation studies using transgenic mice for the efficient detection of point and frame shift mutations (*Mutat. Res.*, 307: 489, 1994; *Mutat. Res.*, 369: 45, 1996).

Dr. Hayashi has extensively summarized and analyzed the data from all the Divisions and has introduced the concept of risk assessment in cancer research to the BSRC (*Toxicol. Indust. Health*, 7: 297, 1991).

The ultimate mission and goal of the BSRC is to play an essential role in regulatory science through its staff's expertise in safety/risk assessment. Regulatory science represents efforts to ensure that products of our advanced technological civilization are developed in harmony with human needs and that the quality, efficacy, and safety of these products are evaluated properly. Evaluation criteria are established through consensus between industry and academia based on thorough scientific discussion. There is a need to develop new evaluation strategies using properly validated methodologies. The essential role of the NIHS is to coordinate regulatory policy and pursue these issues based on the firm belief that such activities are indispensable for optimal human survival.

We are grateful to Dr. Kurokawa and Gary M. Williams for their assistance in the coordination of the material for this cover feature.