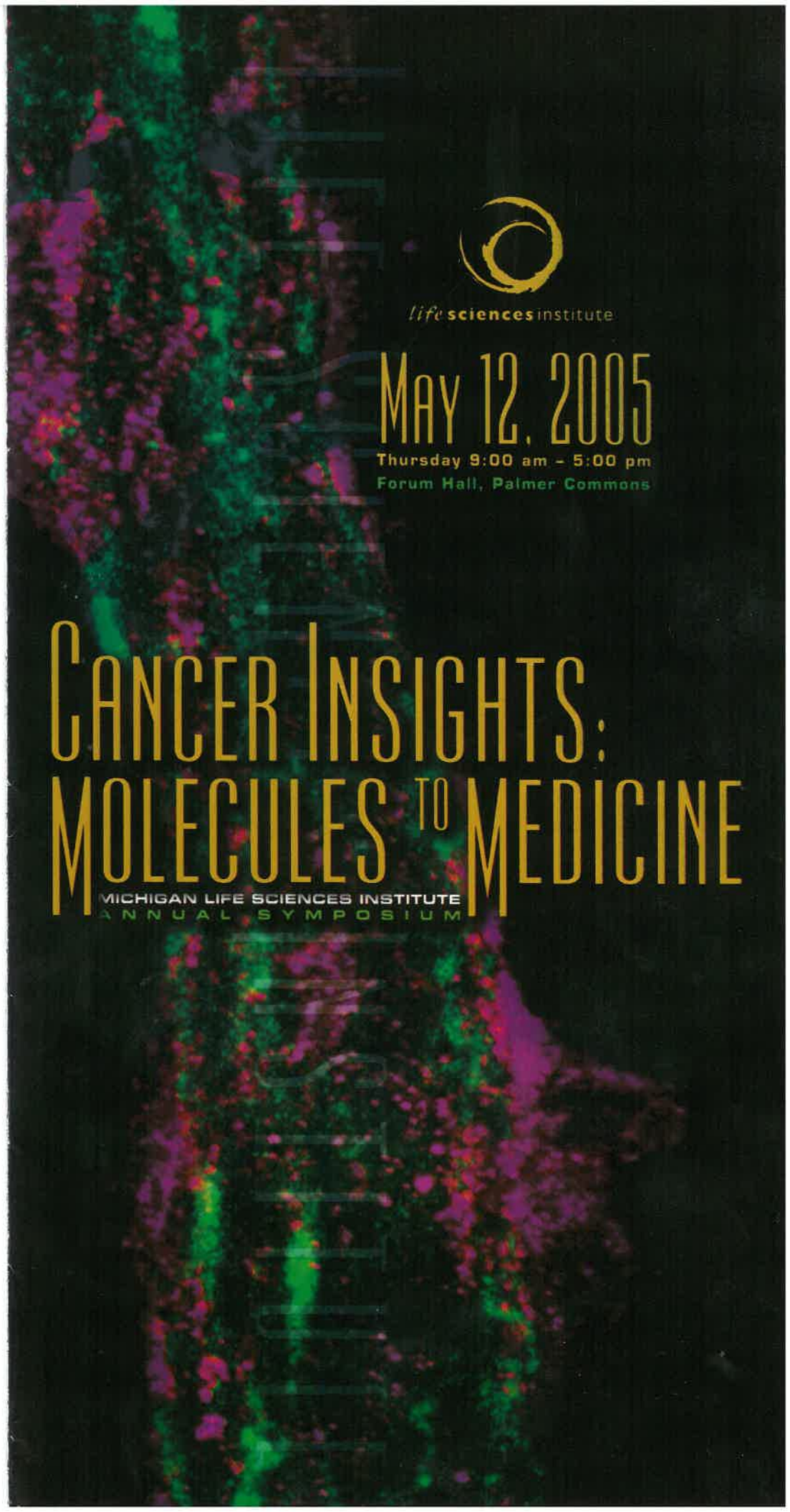
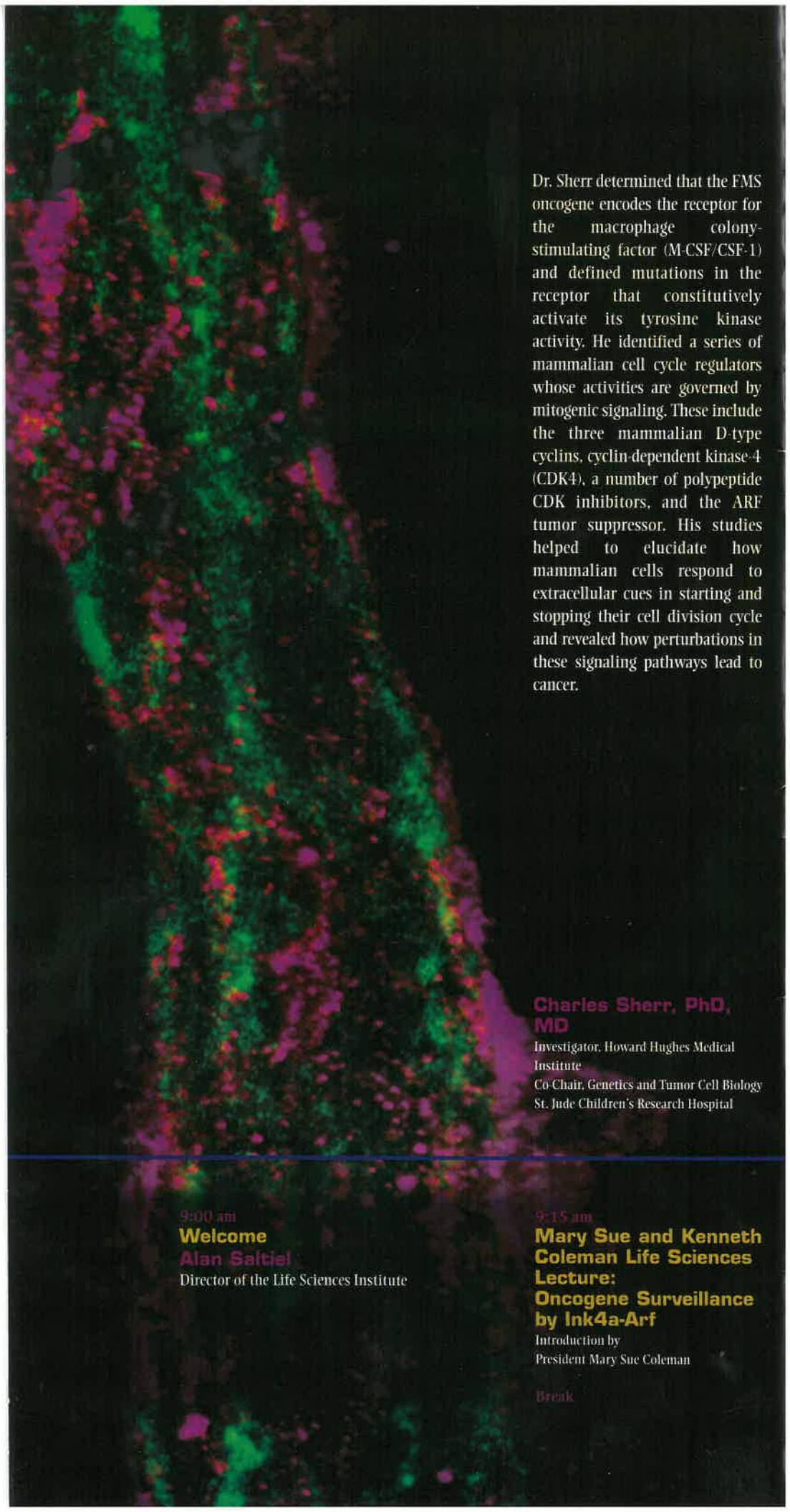

life sciences institute
MAY 12, 2005
Thursday 9:00 am - 5:00 pm
Forum Hall, Palmer Commons
CANCER INSIGHTS:
MOLECULES TO MEDICINE
MICHIGAN LIFE SCIENCES INSTITUTE
ANNUAL SYMPOSIUM



Dr. Sherr determined that the FMS oncogene encodes the receptor for the macrophage colony-stimulating factor (M-CSF/CSF-1) and defined mutations in the receptor that constitutively activate its tyrosine kinase activity. He identified a series of mammalian cell cycle regulators whose activities are governed by mitogenic signaling. These include the three mammalian D-type cyclins, cyclin-dependent kinase-4 (CDK4), a number of polypeptide CDK inhibitors, and the ARF tumor suppressor. His studies helped to elucidate how mammalian cells respond to extracellular cues in starting and stopping their cell division cycle and revealed how perturbations in these signaling pathways lead to cancer.

Charles Sherr, PhD, MD

Investigator, Howard Hughes Medical Institute

Co-Chair, Genetics and Tumor Cell Biology

St. Jude Children's Research Hospital

9:00 am

Welcome

Alan Saltiel

Director of the Life Sciences Institute

9:15 am

Mary Sue and Kenneth Coleman Life Sciences Lecture: Oncogene Surveillance by Ink4a-Arf

Introduction by

President Mary Sue Coleman

Break

Balmain's laboratory focuses on the elucidation of the molecular mechanisms of multistage carcinogenesis, with a particular emphasis on mouse models of chemically induced skin tumor development. He is identifying the sequence of somatic genetic alterations that are associated with discrete stages of tumorigenesis: initiation, promotion, progression to locally invasive lesions and development of metastases. When a genetic change has been identified, he addresses the question of causality by making extensive use of transgenic mice and investigates the biological consequences of this genetic change for cell behavior during transformation. Currently, his laboratory is studying genetic predisposition to cancer, and the relationships between germline susceptibility and tumor suppressor genes. He is extending studies on skin carcinogenesis to other mouse model systems for tumor development in the lung, prostate and lymphoid system.

The Look laboratory is interested in genetic models of leukemogenesis, particularly the highly conserved anti-apoptotic transcriptional pathway downstream of E2A-HLF, a chimeric oncoprotein activated by chromosomal translocation in childhood leukemia. Sequence homology between the HLF transcription factor and CES-2, a cell death specification protein in the nematode Caenorhabditis elegans, suggests that this pathway is not unique to developing B-lymphocytes, but has been evolutionarily conserved in diverse organisms. Recent evidence suggests that this pathway in mammalian cells involves Slug, a zinc-finger transcription factor that is highly related to CES-1, the gene located downstream of CES-2 in the worm. His laboratory is now focusing on the role of Slug in apoptosis, using mice with targeted disruption of the Slug gene. Their goal is to understand pathways of cell death specification in mammals — how they connect to the common machinery of programmed cell death and how they can be disrupted in malignant transformation.

Until recently, Dr. Weber directed a molecular genetics research laboratory focusing on identification and characterization of breast cancer susceptibility genes. Her work in this area included contributions to the mapping and identification of BRCA1 and BRCA2, definition of functional aspects of BRCA1, characterization of the mutational spectrum of BRCA1 and BRCA2 and development of models to use this information to advise women considering genetic testing. Ongoing work in the laboratory is focused on developing methodology to identify novel genes that modify breast cancer risk associated with BRCA1 and BRCA2 mutations and genomic scale characterization of pre-invasive breast lesions, in a continued effort to identify genes that are important in the development of breast cancer. In January 2005 Dr. Weber accepted the position as VP, Translational Medicine and Genetics at GlaxoSmithKline. In her new position, she is extending this work to the development of targeted molecular therapies.

Allan Balmain, PhD, FRSE
Professor, Cancer Research Institute & Biochemistry
University of California

A. Thomas Look, MD
Vice Chair for Research, Pediatric Oncology, Dana-Farber Cancer Institute
Professor of Pediatrics, Harvard Medical School

Barbara Weber, MD
Vice President Translational Medicine & Genetics, Oncology
GlaxoSmithKline

Morning Moderator: Eric Fearon

10:15 am
Mouse Models for the Discovery of Human Cancer Susceptibility Genes

11:00 am
Emerging Genetics of T-ALL — the Role of Notch

Break

Afternoon Moderator: Max Wicha

1:30 pm
Genomic Approaches to Cancer Gene Discovery

Golub's research is focused on the use of genomic approaches to study cancer biology and cancer medicine. His research is based on the premise that extraordinary insights into the molecular basis of cancer can be obtained by taking global views of the genomes of patient-derived tumor samples. Rather than relying exclusively on experimental model systems as the source of discovery, his laboratory relies on naturally arising human tumors. In addition, they are committed to taking global views of cancer genomes that are not constrained by prior assumptions about the nature of cancer pathogenesis.

The Pasqualini laboratory recently observed that blood vessels are strikingly heterogeneous and that blood vessels in tumors are particularly unusual. This understanding assisted in diagnosis and treatment of localized or disseminated (metastatic) cancer. Her laboratory uncovered a novel vascular address system, akin to ZIP codes, on the inner surface of tumor-associated blood vessels that might be used to deliver drugs and other agents selectively to cancers. Other new technology, called in vivo phage display, is now being used to identify the unique molecular addresses of vessels in human cancers. Phage are also being used on blood samples to identify novel tumor markers for the production of anti-cancer vaccines customized for individual cancer patients. Targeting the vasculature of normal and diseased organs may be the foundation of a new pharmacology for the treatment of malignant and inflammatory diseases by delivering drugs to blood vessels.

The Sawyers laboratory studies how molecular abnormalities found in prostate cancer and leukemia lead to abnormal growth and cellular transformation. His research focuses on defining the roles of the PTEN phosphatase, the HER-2/neu receptor tyrosine kinase and the c-myc oncogene in prostate cancer. The results have implications for conducting clinical trials with molecularly targeted agents currently in clinical development. The leukemia studies are focused on signal transduction pathways of the Abl gene and the use of an Abl-specific kinase inhibitor (STI571/Gleevec) that is currently approved for clinical use in patients with chronic myeloid leukemia. His laboratory discovered several different point mutations in the Abl kinase domain that confer drug resistance without impairing kinase activity. Current studies are focused on characterizing the biochemical and biological effects of these mutations on Abl kinase function.

Todd Golub, MD
Investigator, Howard Hughes Medical Institute
Founding Director, Cancer Program, The Broad Institute of MIT & Harvard
Associate Professor of Pediatrics, Dana-Farber Cancer Institute, Harvard Medical School

Renata Pasqualini, PhD
Professor of Medicine & Cancer Biology
The University of Texas MD Anderson Cancer Center

Charles Sawyers, MD
Investigator, Howard Hughes Medical Institute
Director of the Prostate Cancer Program, Jonsson Comprehensive Cancer Center
University of California, Los Angeles

2:15 pm
Genomic Information and Cancer

3:15 pm
Translating Protein Interactions into Targeted Therapies

4:00 pm
Kinase Inhibitors in Cancer Treatment

Break

Improving Human Health Through Collaborative Scientific Discovery

The Life Sciences Institute serves as Michigan's hub for collaborative biomedical research on human health problems. The LSI harnesses the strength and tradition of academic excellence at the University of Michigan by forging links between the health sciences, basic sciences, engineering, the social sciences, and the humanities.

Interdisciplinary science is the feature of LSI's annual symposia. They are designed to encourage the exchange of ideas and to provide the opportunity for students and scientists alike to interact with and learn from prominent scientific leaders about recent developments.

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