Cancer Research Center

About the Center

The Cancer Research Center of Hawai‘i is a research unit that was established as a freestanding independent institute in 1981. When originally conceived and organized in 1971, the Center was part of the Pacific Biomedical Research Center. In its early development the Center was supported by National Cancer Institute (NCI) Planning and Support Grants. In 1979, a construction grant from the NCI together with local matching contributions, supported the erection of a five-story building for the Center in downtown Honolulu. On July 1, 1996, the Center became an NCI-designated center and was awarded the Cancer Center Support Grant. Today, the Cancer Research Center of Hawai‘i continues to bring together researchers who focus on understanding the etiology of cancer and on reducing its impact on the people of Hawai‘i.

Research Programs

The Cancer Etiology Program encompasses both basic laboratory and epidemiologic research. Researchers in this program seek to identify factors, both exogenous and endogenous, that increase or decrease the risk of cancer, and to elucidate the molecular mechanisms that underlie the carcinogenic process. These areas of emphasis reflect the two components of the program: Epidemiology and Molecular Carcinogenesis.

- In the **Epidemiology Section**, researchers explore Hawaii's ethnic diversity and wide variations in cancer incidence rates for clues to cancer etiology. These investigators have a special interest in dietary constituents that may influence the development of cancer, such as fat components, carotenoids, tocopherols, and flavonoids. Potential interactions between the diet and other external factors (e.g., infectious agents like the human papilloma virus and Helicobacter pylori), or host factors (e.g., variant forms of genes that control metabolic processes, such the cytochrome P450 mixed function oxidases) are being intensely studied. Ongoing funded research projects are using case-control and cohort methodologies to test hypotheses related to several different cancer sites, including breast, prostate, colorectum, stomach, cervix, and ovary. Intervention trials to test the potential benefits of particular dietary modifications, such as fat reduction, comprise another active area of research. Most of the epidemiologic research includes major laboratory components that require close interactions with other investigators at the Center, as well as with colleagues at other institutions.

- In the **Molecular Carcinogenesis Section**, researchers are addressing basic questions related to mechanisms of cellular growth control and the disruptions that lead to the development of malignant cells. One focus of this research is on the role of carotenoids and retinoids in increasing gap junctional communication, and of oncogenes and their associated proteins, such as the tyrosine kinases, in decreasing intercellular communication, thereby leading to loss of growth control. Other areas of interest are the mechanisms of action of dietary phytochemicals, such as the tocopherols, that have anti-carcinogenic properties, and the mechanisms by which retinoic acid, vitamin D, and other agents down-regulate the N-myc oncogene in human neuroblastoma.

Most of the research in the Program involves interactions among investigators and laboratories. The epidemiologists rely on collaborations with the molecular biologists, biochemists, nutritionists, biostatisticians, behavioral scientists, and others in order to conduct their research. Several of the epidemiology faculty are participants in a program project grant on diet and cancer. Most investigators in the program also maintain active collaborations with investigators at other universities and cancer centers on the mainland.

The Clinical Sciences Program encompasses the investigation of new approaches to improve the treatment and rehabilitation of cancer patients using pharmacologic, nutritional and psychosocial interventions. An emphasis is on controlling cancer and treatment related symptoms and improving quality of life for cancer patients and survivors in Hawaii's multiethnic population. Furthermore, the Program

encompasses the investigation of pharmacologic and nutritional interventions for reducing the incidence of cancer.

Three lines of investigation provide a framework for the Program's innovative research.

1. A comprehensive investigation of psychosocial and behavioral influences on the well being of cancer patients, their families and significant others over the continuum of care from initial diagnosis to long term survivorship.
2. An investigation of the patterns of use and the efficacy and toxicity of selected Complementary and Alternative Medicine (CAM) practices with a special focus on techniques derived from the healing traditions of Asians, Pacific Islanders and other groups comprising Hawaii's multiethnic population.
3. An investigation of dietary modifications and nutrition related interventions that may reduce the risk of cancer development and progression.

Through its Clinical Trials Unit, the Clinical Sciences Program enrolls subjects in over one hundred active, National Cancer Institute (NCI) sponsored, and industry sponsored multi-center studies. NCI support for national clinical trials is predominantly through a Minority-Based, Community Clinical Oncology Program (CCOP) award. The Clinical Sciences Program includes the NCI supported Cancer Information Service (CIS) of Hawaii which partners with community agencies to provide cancer information and community education throughout the islands.

Natural Products Program: The overall objective of the Natural Products Program is to foster collaborative research leading to the discovery and development of new drugs for the treatment of cancer. The Program emphasizes the systematic evaluation of the unique biota of the Indo-Pacific region as a source of molecular diversity, and combines chemistry and biology components in a manner that bridges the gaps between traditional academic disciplines to enhance collaborative interactions. The specific goals of the Natural Products Program are:

- To discover and characterize new chemotherapeutic agents, emphasizing natural products.
- To investigate drug mechanisms at the biochemical, molecular and genetic levels.
- To develop innovative new molecular targets and assays for small molecules, taking advantage of recent advances in cancer biology.
- To discover innovative new techniques that might be used to design and synthesize drugs, including both chemical and biological production.
- To translate the results of basic laboratory research into more effective cancer therapies.

The Natural Products Program, formally organized in 1990, developed as a result of long-standing interactions between investigators who combined their diverse interests in pharmacology, cancer biology, organic chemistry, botany, and microbiology, as well as a strong common interest in cancer therapeutics, to address the pressing need for new cancer drugs having specific effects on tumor cells and no side effects on normal tissues. Currently, the Program includes six full members who have their primary academic appointments in four different units of the University of Hawaii (Department of Chemistry, Department of Botany, CRCH, and the Pacific Biomedical Research Center) and one affiliate member. The Program is a multidisciplinary research/drug discovery group that functions in separate but interrelated and interdependent areas: the acquisition of new, untested source material for screening; the development and implementation of innovative mechanism-based, cancer-relevant bioassays; the isolation and identification of active compounds; and, for those pure compounds active in vitro, both detailed pharmacological investigation and definitive in vivo evaluation. Translation of these research results into clinical trials is accomplished through partnerships with private industry.

The Social and Behavioral Sciences Program is a new program, and was formally established in July of 2001 as a Developing Program at the Cancer Research Center of Hawaii. The Social and Behavioral Sciences Program focuses on applications of social science research methods, including theories of human behavior and rigorous measurement, to preventing cancers and detecting them in an early stage, when they are most treatable. Several interrelated areas of focus are central to the program: health of children, youth and families; high-risk groups and risk communication; ethnic differences; social policy issues; and

innovative communication technology. Areas for expanded future focus include interactive health communications and cancer related health disparities.

In ongoing research in this program, these foci are currently applied to behaviors and environments related to tobacco use, skin cancer, colorectal cancer detection, genetic testing, alcohol consumption, and dietary change.

The program emphasizes community-based research that involves strong collaborative relationships with individuals and groups in Hawaii and elsewhere. A hallmark of our research is its multi-sectoral collaborations with education, health care, public health, law enforcement, and social service agencies. Our community research extends to all regions of the state of Hawaii, and all current studies in the state include both Oahu and Neighbor Island participants and agency partners.

This Program will expand and venture into new areas with the addition of more active investigators. Recruitments for three new faculty members are currently in progress in late 2001.

Basic Laboratory Science Research

Basic laboratory science research at the Cancer Center is performed by independent investigators, who employ cellular and molecular biological approaches to study the mechanisms regulating cellular neoplastic transformation, cell growth, gene regulation, and apoptosis. Collaborative efforts are also underway to identify novel modulators of oncogene proteins and cytoskeletal elements from blue-green algae and higher plant natural products. Participating investigators are members of the *Molecular Carcinogenesis Section (*Cancer Etiology*)* or *Natural Products Programs* of the Cancer Center. The research is performed in modern, well-equipped laboratories, which are located on the third floor of the Cancer Research Center. The close proximity of the laboratories and their staff provide generous opportunities for the interaction of personnel and the interchange of concepts and information.

Research training opportunities are provided by these laboratories for advanced high school, undergraduate and graduate students and postdoctoral fellows yearlong and during the summer months. Undergraduate students in MARC, or MBRS (Haumana) training programs at the University of Hawaii's Manoa campus or Chaminade University perform directed research projects. Graduate students from departments in the Medical School and the newly established *Cell and Molecular Biology graduate program* engage in laboratory rotations or Ph.D. dissertation research under these laboratory investigators. Numerous postdoctoral fellows from national and international origins obtain advanced laboratory training in the Center's facilities. Support of graduate or postdoctoral students working in a laboratory is provided by the laboratory head. The basic science faculty have joint appointments in the Departments of Genetics and Molecular Biology or Biochemistry and Biophysics at the John A. Burns School of Medicine. The research training experience of students at the Cancer Center is enriched by formal coursework offered by various undergraduate and graduate departments on the University of Hawaii Manoa campus, seminar series organized by the Center and University, as well as several individual journal clubs offered by various basic science faculty.

Scientific instrumentation at the Cancer Center is maintained and serviced by an in-house technician operating from the Shared Instrumentation Resource. The Center's laboratory research activities are supported by the Molecular Biology Facility on the University of Hawaii Manoa campus, which provides automated DNA and protein sequencing, oligonucleotide and peptide synthesis, amino acid composition analysis, and molecular modeling services. The main research library (Hamilton) is also located on the Manoa campus, which is easily accessed in approximately 20 minutes from the Center by a newly established CityExpress! bus route. Pertinent research journals subscribed to by Hamilton library or the Cancer Center can be accessed through the Internet by a state of the art, fiber optic computer network, which services all laboratories in the Center. The Hawaii Medical Library and the Queen's Medical Center, the main tertiary care facility in Hawaii, are adjacent to the Cancer Center and offer additional basic science and clinical journals and sponsor clinically-oriented seminars.

Cancer Control Research Training in Multiethnic Hawaii

This cancer control research training program is aimed at training scientists with doctorates to conduct independent cancer control research. It will be led by population researchers representing the disciplines of behavioral sciences, epidemiology, nutrition, and biostatistics; and based at the Cancer Research Center of Hawaii (CRCH) at the University of Hawaii.

Postdoctoral trainees will complete a two year training program, which will include multiple mentors, formal curricular activities, research seminars, journal clubs, and hands-on research activity. Individualized training program objectives and plans will be developed based on the trainee's prior academic preparation and career goals. Interaction with the interdisciplinary program faculty, and with other trainees, will be integral to the training experience. Methodological and substantive topics related to cancer control research in ethnic minorities will be emphasized throughout the program. A special Asian/Pacific Islander/Native Hawaiian Studies track will be available to trainees who are pursuing careers where they will work mainly with these ethnic groups. The training experience will culminate in development of a mock NIH application *for a career development award or a research project grant*, and an accompanying mock peer review experience.

The program faculty are actively engaged in conducting population science research in Hawaii and with collaborating research sites elsewhere in the United States and abroad. Their work emphasizes understanding cancer causation, prevention, and control in Hawaii's ethnically diverse populations; and identifying and evaluating strategies for reducing cancer-related health disparities in incidence, morbidity, and mortality. This training environment, together with the proposed Program plan, provides an ideal opportunity for quality career development for cancer control scientists in the twenty-first century.

Extramural Funding
Research Awards: 57 Grants, $15,960,951
Nonresearch Awards: 9 Grants, $1,022,332

Faculty Profile

Publications and Presentations
274 Publications, over 100 presentations.

Faculty Awards and Honors
- Professorship of Survivorship Award, 2001 Susan G. Komen Breast Cancer Foundation: Carolyn Gotay.
- Award for Excellence in Education for the Local, State, Regional and National Professional Society/Organization, American Academy of Dermatology, 2000: Karen Glanz

Research Projects
Dr. Kolonel has developed and sustained a world-renowned program in cancer epidemiology that has served as the base of strength for the development of the Cancer Research Center. In particular, as principal investigator of the only NIH Program Project Grant in the State of Hawaii, he has successfully initiated an ambitious program studying the relation of diet, genetics and cancer. The current award of $14,000,000 over 5 years continues this research first initiated as a Program Project in 1982 and has been continuously funded over the last 20 years.

The Cancer Research Center has gained recognition as an important locus of research in the field of gap-junctional cellular communication. Dr. Alan Lau, Dr. John Bertram and Dr. Bonnie Warn-Cramer currently study various aspects of this cellular phenomenon related to growth control and cancer. In 2001 Dr. Lau chaired and hosted the International Meeting of cellular gap junction researchers here in Hawaii with an attendance of 350 renowned researchers from around the world.

Four researchers are studying various aspects of the biology and treatment of neuroblastoma at the Cancer Research Center. They include Dr. Carl-Wilhelm Vogel, Dr. Randy Wada, Dr. Andre Bachman, and Dr. David Fritzinger. They are leaders in their field elucidating the role of oncogene regulation and immunology in the progression of this devastating childhood disease.

Activating Multiethnic Youth for Smoking: Through the Social and Behavioral Sciences Program. Prevention is underway in 22 middle schools in Hawaii, involving 3,765 students. The Study, known as SPLASH, has been using an internet-based virtual classroom and drama education in the 7th grade to encourage youth to become advocates for anti-smoking efforts. Results of the pilot study in three schools showed that both the innovative intervention and the control treatment (usual care) were feasible and well received by teachers and students. Project SPLASH recently expanded with the award of a Native Hawaiian Supplement from the National Cancer Institute and a new dissemination grant from the state's Tobacco Trust Advisory Board. Because Native Hawaiians have the highest rates of tobacco use in the state, prevention is especially important in this ethnic group. The Native Hawaiian Supplement supports testing of a culturally adapted version of the Project SPLASH intervention in both public and private schools where most or all of the students are of Native Hawaiian ancestry. The adaptation includes articulation of cultural values compatible with nonsmoking lifestyle (e.g. malama 'aina, kokua) and the use of Native Hawaiian role models as advocates for health promotion and environmental protection.

Natural Products research takes advantage of our unique location in the Pacific to detect, isolate and identify promising new therapeutic agents from the diverse flora and fauna of the tropical Pacific. This program brings together chemists, molecular biologists, botanists, and microbiologists in the process of identifying lead compounds from organisms found in our unique environment. Cryptophycin, a potent anti-tumor agent was discovered in cyanobacteria by UH researchers and has reached the level of a phase-two technical trial. Its discovery and subsequent research led to one of the most successful commercial agreements in UH history.

Community Service Projects

- Cancer Information Service
- Clinical Trials Unit
- Tumor Registry
- Annual Community Service Project