

EXTRAMURAL GRANTS

American Cancer Society

Total Grants In Effect On 7/1/2005

Total Number of Grants:

818

Total Amount of Grants:

\$411,678,147

GRANT LISTING IS ON NEXT PAGE

EXTRAMURAL GRANTS

American Cancer Society
Grants in effect on 7/1/2005

Page: 1

Grant No.	Investigator/Institution	Title	Term	Amount
Connecticut				
RSG-05-222-01 (CDD)	Braddock, Demetrios T., M.D., Ph.D. Yale University Department of Pathology 310 Cedar Street New Haven, CT 06520-8023	Molecular Determinants of Nucleic Acid Recognition by KH Domains	7/1/2005 through 6/30/2009	720,000
TURSG-01-174-01 (MBC)	Brandsma, Janet L, Ph.D. Yale University Section of Comparative Medicine LSOG 117 333 Cedar Street New Haven, CT 06520-8016	Vaccination Against Papillomavirus-Induced Disease	7/1/2001 through 6/30/2006 Funds ended 06/30/05	879,000
RSG-04-031-01 (CCE)	Cao, Deliang, M.D., Ph.D. Yale University Department of Internal Medicine 333 Cedar Street New Haven, CT 06520	Mechanisms Affecting Fluoropyrimidine Activity and Tumor Selectivity	1/1/2004 through 12/31/2007	720,000
RSG-05-146-01 (LIB)	Czyzyk, Jan K., M.D. Yale University Department of Pathology LH-20 310 Cedar Street New Haven, CT 06510	Alternative Effectors of Ras GTPase in T Cell Activation	7/1/2005 through 6/30/2009	720,000
RSG-02-034-01 (CCG)	DiGiovanna, Michael P., M.D., Ph.D. Yale University Department of Internal Medicine P.O. Box 208032 New Haven, CT 06520-8032	Targeting HER2 and Estrogen Receptor in Breast Cancer	1/1/2002 through 12/31/2005	989,000
IRG-58-012-48 (IRG)	Edelson, Richard, M.D. Yale University Yale Comprehensive Cancer Center Room 205 WWW 333 Cedar Street New Haven, CT 06520-8028	Institutional Research Grant	1/1/2005 through 12/31/2007	420,000

EXTRAMURAL GRANTS

American Cancer Society
Grants in effect on 7/1/2005

Page: 2

Grant No.	Institution	Title	Term	Amount
Connecticut				
DSCN-04-164-01 (SCN)	Haozous, Emily A., BA, RN, MSN Mentor: Knobf, M. Tish, Ph.D., R.N. Yale University Adult Advanced Practice Program 100 Church Street, South P.O. BOX 9740 New Haven, CT 06519-0740	Understanding the Cancer Pain Experience in Southwestern Native Americans	8/1/2004 through 7/31/2006	30,000
MRS-04-006-01 (CPPB)	Irwin, Melinda L., Ph.D., M.P.H. Yale University Department of Epidemiology and Public Health P.O. Box 208034 New Haven, CT 06520-8034	Exercise Intervention in Breast Cancer Survivors	1/1/2004 through 12/31/2006	434,000
PF-03-127-01 (LIB)	Li, Ming, Ph.D. Mentor: Flavell, Richard A., Ph.D. Yale University Section of Immunobiology 300 Cedar Street TAC S-569 New Haven, CT 06520	Function of Phosphatidylserine Receptor in T Cell Development	7/1/2003 through 6/30/2006	124,000
PF-04-244-01 (CSM)	Mackey, Andrew T., Ph.D. Mentor: Mooseker, Mark S., Ph.D. Yale University Department of Molecular, Cellular and Developmental Biology KBT 352 219 Prospect Street New Haven, CT 06511	Mutational Analysis of the Intestinal Epithelial Brush Border	12/1/2004 through 8/31/2007	112,500
PF-05-227-01 (GMC)	Macris, Margaret A., Ph.D. Mentor: Sung, Patrick, Ph.D. Yale University Department of Molecular Biophysics and Biochemistry SHM C1304 333 Cedar Street New Haven, CT 06520-8024	Role of the RecQ4/RTS Helicase in Genome Maintenance	7/1/2005 through 6/30/2008	138,000

EXTRAMURAL GRANTS

American Cancer Society
Grants in effect on 7/1/2005

Page: 3

Grant No.	Investigator/Institution	Title	Term	Amount
Connecticut				
PTAPM-04-081-01 (PTAPM)	Nawaz, Haq, M.D., M.P.H. Griffin Hospital Department of Medical Education 130 Division Street Derby, CT 06418 TRAINEE: Khubchandani, Sapna, M.D. 46 Hickory Lane Waterford, CT 06385	Physician Training Award in Preventive Medicine	1/1/2004 through 12/31/2007	300,000
RSG-02-050-01 (GMC)	Peng, Zheng-Yu, Ph.D. University of Connecticut Health Center Department of Biochemistry MC-3305 263 Farmington Avenue Farmington, CT 06030	Structural Consequences of Cancer-Derived Mutations in Tumor Suppressor p16	1/1/2002 through 12/31/2005	796,000
RSG-03-058-01 (LIB)	Shlomchik, Warren D., M.D. Yale University Department of Internal Medicine WWW 217 333 Cedar Street New Haven, CT 06520	Analysis of Alloimmunity to CML in a Novel Murine Model	1/1/2003 through 12/31/2006	734,000
MRS GT-05-003-01 (CPHPS)	Soler-Vila, Hosanna, Ph.D. Mentor: Jones, Beth A., Ph.D., M.P.H. Yale University Department of Epidemiology and Public Health Room 438, 60 College Street P.O. Box 208034 New Haven, CT 06520-8034	Psychosocial Factors, Race, and Cancer Survival	1/1/2005 through 12/31/2009	647,000
RSG-02-052-01 (GMC)	Strobel, Scott A., Ph.D. Yale University Molecular Biophysics and Biochemistry 266 Whitney Avenue P.O. Box 208114 New Haven, CT 06520-8114	Mechanism and Inhibition of Ribosomal Protein Synthesis	1/1/2002 through 12/31/2005	899,000

EXTRAMURAL GRANTS

American Cancer Society
Grants in effect on 7/1/2005

Page: 4

Grant No.	Investigator/Institution	Title	Term	Amount
Connecticut				
RSG-03-246-01 (MBC)	Sun, Hong, Ph.D. Yale University Department of Genetics 333 Cedar Street New Haven, CT 06520	Using C .Elegans Model System to Dissect PI 3-kinase/PTEN Signaling Pathway	7/1/2003 through 6/30/2007	720,000

Totals for State

Number of Grants: 17
Total Amount of Grants: 9,382,500

Grant Profile Information

Demetrios T. Braddock, M.D., Ph.D.

Molecular Determinants of Nucleic Acid Recognition by KH Domains

Yale University
Department of Pathology
310 Cedar Street
New Haven, CT 06520-8023
203-737-1278 (phone)
203-785-7303 (fax)
demetrios.braddock@yale.edu

Grant No. RSG-05-222-01-CDD
Division New England
Term of Grant: 7/1/2005 - 6/30/2009
Total Award: \$ 720,000
Total ACS Support: \$ 720,000

Priority Areas:

Organ Sites:	Breast	20%
	Cervix - uterine	5%
	Colon - rectum	20%
	Liver	20%
	Lung	10%
	Non-Hodgkin's Lymphoma	20%
	Ovary	5%

Special Categories:

Project Summary

The dysregulated expression of the oncogene *c-myc* is among the most frequent molecular abnormalities associated with cancer. The *c-myc* gene is amplified in lung, breast, liver, cervical, ovarian, and colon cancer, as well as malignancies of the lymphatic system. The Fuse Binding Protein (FBP) is essential for *c-myc* gene regulation and controls expression of *c-myc* by binding to DNA in front of the gene at a DNA sequence termed FUSE. FBP recognizes its target DNA sequences via modules in the protein called K homology (KH) repeats. An interfering signal comprised of the KH domains of FBP stops cell growth and shuts down *c-myc* expression in cancer cells grown in cell cultures. A possible means of control for tumors driven by the *c-myc* oncogene may therefore be small molecules which can interfere with FBP's interaction with DNA. We propose to study the details of the parts of KH domain interaction with nucleic acids and note that this knowledge is a prerequisite for the development of small molecule inhibitors which would limit *c-myc* expression and cell growth. The KH domains of FBP, when transfected into tumor cells driven by *c-myc*, stop cell growth and shut down *c-myc* expression (He, Liu et al. 2000). The rules for how KH domains accomplish the molecular recognition of nucleic acids are yet to be determined, and are of fundamental biological importance. Determining these rules is the central aim of this project.

Grant Profile Information

Research Promotion Information

Demetrios T. Braddock, M.D., Ph.D.

Grant No. RSG-05-222-01-CDD

Hometown (currently reside): Springfield, Illinois

Publications suggested by grantee to receive an ACS grant press release:

Springfield Journal Register, Springfield Il.

Yale Medicine

University of Chicago Magazine

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Janet Rettig Emanuel, Ph.D. - 203-432-2157

Grant Profile Information

Janet L Brandsma, Ph.D.

Vaccination Against Papillomavirus-Induced Disease

Yale University
Section of Comparative Medicine
LSOG 117
333 Cedar Street
New Haven, CT 06520-8016
203-785-4401 (phone)
203-785-7499 (fax)
janet.brandsma@yale.edu

Grant No. TURSG-01-174-01-MBC
Division New England
Term of Grant: 7/1/2001 - 6/30/2006
Total Award: \$ 879,000
Total ACS Support: \$ 879,000

Priority Areas:	Early Detection Diagnosis and Prognosis	10%
	Scientific Model Systems	40%
	Treatment	50%
Organ Sites:	Cervix - uterine	100%

Special Categories: Socio-economically Disadvantaged or Special Populations

Project Summary - Next Page

Grant Profile Information

Human papillomavirus (HPV) infection of the uterine cervix can lead to cervical cancer, the most common female cancer in developing countries. In the US, poor and medically underserved women have higher rates of cervical cancer than other women. An effective HPV vaccine should induce long-term immunologic protection against HPV infection and premalignant disease, and would provide a cost-effective method for preventing cervical cancer worldwide. This project will test a novel "prime-boost" vaccination strategy that has been shown to induce greatly heightened specific immunity against other human pathogens. The strategy will be to prime an immune response with a DNA vaccine and boost it later with live virus vaccine targeting papillomavirus proteins. Because the cottontail rabbit papillomavirus (CRPV)-rabbit model is the only animal model of high-risk papillomavirus infection, vaccines targeting this virus will be used. The CRPV DNA vaccine to be used protects against CRPV infection and has some therapeutic effects on established lesions. A CRPV live virus vaccine will be generated using a vesicular stomatitis virus (VSV) vector that has been used successfully in other virus systems. Clinical outcomes in vaccinated rabbits will determine if priming with the DNA vaccine and boosting with the VSV vaccine induces superior prophylactic and therapeutic immunity compared to priming and boosting with either vaccine alone. Laboratory assays to test vaccinated and infected rabbits for cellular immune responses to the virus will be developed using dendritic and lymphoid cells from inbred rabbits. These and other assays will be used to test for correlations between CRPV-specific immune responses and vaccine-induced effects on papilloma formation and papilloma regression. Positive correlations will suggest immunologic mechanisms that cause protection/regression. Data analysis also could identify needed immunologic markers for predicting the efficacy of vaccination in individuals before exposure to the virus. The results of these studies are expected to provide a rationale for the development of HPV early gene vaccines to treat HPV-associated disease in humans.

Grant Profile Information

Research Promotion Information

Janet L Brandsma, Ph.D.

Grant No. TURSG-01-174-01-MBC

Hometown (currently reside): Guilford, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Grantee willing to discuss your projects with the media? N/A

Grantee willing to discuss to speak at ACS sponsored events? N/A

Grantee willing to serve as an expert or as a member of a speaker's bureau? N/A

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Grant Profile Information

Deliang Cao, M.D., Ph.D.

Mechanisms Affecting Fluoropyrimidine Activity and Tumor Selectivity

Yale University
Department of Internal Medicine
333 Cedar Street
New Haven, CT 06520
203-785-4388 (phone)
203-785-7670 (fax)
deliang.cao@yale.edu

Grant No. RSG-04-031-01-CCF
Division New England
Term of Grant: 1/1/2004 - 12/31/2007
Total Award: \$ 720,000
Total ACS Support: \$ 955,000

Priority Areas:	Scientific Model Systems	50%
	Treatment	50%
Organ Sites:	Breast	50%
	Colon - rectum	50%

Special Categories:

Project Summary - Next Page

Grant Profile Information

Cancer represents one of the leading causes of mortality in the Western world. In many patients at diagnosis, the disease has already spread to other organs including bone marrow, therefore limiting the success of surgical intervention and radiation therapy. For most of the patients, chemotherapy remains the only treatment available even though the systemic toxicity linked to most of the chemotherapeutic agents currently in use represents a major drawback. Thus, more selective mode of treatment or "rescue" regimens have to be developed to improve the quality of life of the patients and allow a more intense drug dosage. Large doses of uridine or uridine phosphorylase (UPase) inhibitor, such as benzylacetylouridine (BAU), have been proven to efficiently rescue 5-fluorouracil (5-FU)-induced host toxicity and therefore improve the therapeutic index of this drug. Our recent study has further demonstrated that the abrogation of UPase activity could reduce 10- and 16-fold of cell sensitivity to 5-FU and 5-deoxy-5-fluorouridine (5-DFUR), respectively. Using UPase knockout model that we have generated, therefore, we will further determine in vivo the effect of UPase on host toxicity, antitumor activity, and tumor selectivity of fluoropyrimidines (such as 5-FU and capecitabine) used currently for treatment of metastatic breast and colorectal cancers. We will also define the role of UPase in uridine homeostatic regulation and uridine "rescue" using this knockout model. In addition, UPase has been found induced in a wide range of human tumor types and its expression is regulated by both the tumor suppressor gene p53 and the oncogene c-H-ras. These two genes are frequently altered in human cancers. To directly translate the findings of this study into clinical application, we will retrospectively investigate a number of clinical cases. On a collection of 152 human breast and more than 100 colon tumor specimens and the matched normal tissues, we will systemically analyze UPase expression and p53 (a suppressor of UPase gene expression) mutations as well as their relationship to determine their implication on 5-FU based therapy. These studies will provide valuable information for the individualization of the antitumor regimens and for the design of new therapeutic strategies.

Grant Profile Information

Research Promotion Information

Deliang Cao, M.D., Ph.D.

Grant No. RSG-04-031-01-CCE

Hometown (currently reside): Cheshire, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

New Haven Register

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Renee Moore

Grant Profile Information

Jan K. Czyzyk, M.D.

Alternative Effectors of Ras GTPase in T Cell Activation

Yale University
Department of Pathology
LH-20
310 Cedar Street
New Haven, CT 06510
203-785-5400 (phone)
203-737-1765 (fax)
jan.czyzyk@yale.edu

Grant No. RSG-05-146-01-I.IB
Division New England
Term of Grant: 7/1/2005 - 6/30/2009
Total Award: \$ 720,000
Total ACS Support: \$ 720,000

Priority Areas:

Organ Sites:	Brain	20%
	Leukocytes	80%

Special Categories:

Project Summary - Next Page

Grant Profile Information

The most important factor in the ability of the immune system to defend our organism from infectious agents is a class of white blood cells called T lymphocytes. These cells bind antigens through the specific antigen receptors on the surface. In addition, T cells are equipped with the surface receptors called integrins, which are responsible for the physical contacts between T lymphocytes and other cell types. Both antigen binding and integrin-mediated interactions greatly influence the ability of T cells to divide and secrete hormone-like growth factors called cytokines, which in turn stimulate other elements of the immune system. In patients with leukemia, lymphocytes proliferate independently of antigen stimulation, and through integrin-mediated contacts rapidly disseminate in the body. It is thought that integrins accelerate metastatic phase of neoplastic process by assisting tumor cells to migrate from the blood through the vascular wall into adjacent tissue sites. Our research plan aims to study molecule called Ras which resides inside T lymphocytes. When T cells encounter their antigen, Ras is rapidly turned on and increases the ability of T lymphocytes to divide and secrete cytokines. Furthermore, some studies suggest that Ras is responsible for activation of integrin receptors. Hence, for several reasons Ras appears to be important in programming T lymphocytes to grow, proliferate, and migrate. Importantly, constitutively active forms of Ras are commonly found in a wide spectrum of human hematologic disorders including myelodysplastic syndromes, juvenile myelomonocytic leukemia, and T-cell acute lymphoblastic leukemia. In this grant we will study how Ras and its recently discovered partner, termed phospholipase C-epsilon (PLCe), control activation of T cells. More specifically, we will analyze action of Ras and PLCe on integrins. In order to accomplish this objective, we will use a virus as vehicle to infect and deliver artificially active form of Ras, and examined whether this compound can potentiate function of integrin receptors. Next, T cells carrying active Ras will be injected into mice and examine for organ distribution. In this way, we hope to be able to better understand how Ras controls lymphocyte traffic in the body. Finally, we will suppress the level of PLCe in T cells and examine whether this change results in defective action of integrins. The central role of T cells justifies efforts to discover new drugs which would keep this class of cells in check. In keeping with this, conclusions reached under this proposal will form a baseline for future work attempting to develop selective blockers of Ras and PLCe. When used against T lymphocytes, these blockers might have potential to inhibit development of lymphoproliferative malignancies.

Grant Profile Information

Research Promotion Information

Jan K. Czyzyk, M.D.

Grant No. RSG-05-146-01-LIB

Hometown (currently reside): Hamden, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Hamden Chronicle

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

John West - 203-785-5987

Grant Profile Information

Michael P. DiGiovanna, M.D., Ph.D.

Targeting HER2 and Estrogen Receptor in Breast Cancer

Yale University
Department of Internal Medicine
P.O. Box 208032
New Haven, CT 06520-8032
(203) 737-5240 (phone)
(203) 785-7531 (fax)
michael.digiovanna@yale.edu

Grant No. RSG-02-034-01-CCG
Division New England
Term of Grant: 1/1/2002 - 12/31/2005
Total Award: \$ 989,000
Total ACS Support: \$ 989,000

Priority Areas:	Biology	50%
	Treatment	50%
Organ Sites:	Breast	100%

Special Categories:

Project Summary

The drug tamoxifen works by preventing estrogen from binding to the estrogen receptor (ER), so that estrogen, a "growth factor" for breast cancer, cannot stimulate its growth. Finding similar drugs to inhibit other growth factors, that don't have side effects of conventional chemotherapy, is a high priority. HER2 is a different type of growth factor receptor also crucial in inflammatory breast cancer, and for which the monoclonal antibody Herceptin is now available to inhibit its function and treat breast cancer patients. Remarkably, studies of the biology of ER signals and HER2 signals have shown that the two intimately interact with each other. We hypothesize that combining drugs that inhibit both HER2 and ER will have a synergistic effect on breast cancer. We will test this hypothesis, and study the mechanisms of what happens inside cells when both are inhibited. Curiously, despite the fact that both interact and stimulate breast cancer growth, HER2 and ER seem to be antagonistic, in that high levels of one tends to turn down levels of the other; this may suggest that while breast cancer needs at least one of these, having both active may be bad for a breast cancer. We will also therefore examine what happens when both are simultaneously stimulated, as an alternative strategy to treat breast cancer. We propose to use breast cancer cells with varying levels of HER2 and ER to: 1) test the effect of combining drugs that inhibit HER2 and ER, 2) test the effects of combining drugs that are inhibitors or stimulators of HER2 and ER, and 3) test these treatments in mice with breast cancer. Beside elucidating this important biologic aspect of breast cancer, the results of these studies would be immediately applicable to the treatment of breast cancer patients.

Grant Profile Information

Research Promotion Information

Michael P. DiGiovanna, M.D., Ph.D.

Grant No. RSG-02-034-01-CCG

Hometown (currently reside): North Haven, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Yale Alumni Magazine, The New Haven Register, The Hartford Courant

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Renee Moore

Grant Profile Information

Richard Edelson, M.D.

Institutional Research Grant

Yale University
Yale Comprehensive Cancer Center
Room 205 WWW
333 Cedar Street
New Haven, CT 06520-8028
203-785-4095 (phone)
203-785-4116 (fax)
richard.edelson@yale.edu

Grant No. IRG-58-012-48-IRG
Division New England
Term of Grant: 1/1/2005 - 12/31/2007
Total Award: \$ 420,000
Total ACS Support: \$2,692,750

Priority Areas:

Special Categories:

Project Summary

The purpose of the IRG (Institutional Research Grant) is to provide "seed" money awards for the initiation of promising new projects by junior faculty members (or their equivalents), so they can obtain preliminary results that will enable them to compete successfully for national research grants. IRGs are intended to support independent, self-directed investigators early in their careers, for whom the institution must provide research facilities or space customary for an independent investigator.

Since an IRG is awarded to an institution as a whole, funds should be available to support proposals from all health sciences schools, colleges, and departments. Institutions are encouraged to partner with other institutions that are in the same geographical area, that would not on their own have a sufficiently large pool of junior faculty to apply for an IRG.

Grant Profile Information

Research Promotion Information

Richard Edelson, M.D.

Grant No. IRG-58-012-48-IRG

Hometown (currently reside):

Publications suggested by grantee to receive an ACS grant press release:

New Haven Register

Yale Cancer Center Newsletter

Yale Bulletin

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Renee Gaudette - 785-2143

Grant Profile Information

Emily A. Haozous, BA, RN, MSN

Understanding the Cancer Pain Experience in Southwestern Native Americans

Yale University
388 Whitney Avenue, #3
New Haven, CT 06511
203 497-9566 (phone)
emily.haozous@yale.edu

Grant No. DSCN-04-164-01-SCN
Division New England
Term of Grant: 8/1/2004 - 7/31/2006
Total Award: \$ 30,000
Total ACS Support: \$ 30,000

Priority Areas: Cancer Control Survivorship and Outcomes Research 100%

Special Categories: Socio-economically Disadvantaged or Special Populations

Project Summary

As many as eighty percent of cancer patients experience pain as a result of their cancer, with pain intensity increasing with severity of cancer in the individual. Research suggests that minorities are consistently undertreated for pain. Due to high mortality rates from cancer for among Native Americans, it can be concluded that many Native Americans with cancer suffer from poorly managed pain. While there is an existing body of knowledge about other minority groups and cancer pain, pain in Native Americans remains poorly understood. Research that clarifies the cancer pain experience for Native Americans would assist in improving the quality of life for those people living with cancer and cancer pain. The purpose of this study is to explore and compare the cancer pain experience in a population of Native Americans in northern New Mexico. Part of understanding the experience includes exploring barriers to main management as seen by both the patient and the care provider. This study will interview cancer patients living within the Eight Northern Pueblos Intertribal Consortium of Native American communities in northern New Mexico, and care providers to try to understand the current pain management for Native Americans with cancer in these communities. The findings from this study will help determine barriers to treatment as well as the meaning and significance of pain to the people experiencing it. By interviewing individuals from a variety of different Native American communities, the results can be used to develop better means for managing cancer pain for these communities in the future. As knowledge of the Native American cancer pain experience increases, health care providers will be better prepared to treat their Native American cancer patients in a way that is respectful and effect for those patients.

Grant Profile Information

Research Promotion Information

Emily A. Haozous, BA, RN, MSN

Grant No. DSCN-04-164-01-SCN

Hometown (currently reside): New Haven, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Ilya Sverdlov - 203-737-1376

Grant Profile Information

Melinda L. Irwin, Ph.D., M.P.H.

Exercise Intervention in Breast Cancer Survivors

Yale University
Department of Epidemiology and Public
Health
P.O. Box 208034
New Haven, CT 06520-8034
203-785-6392 (phone)
203-785-6279 (fax)
melinda.irwin@yale.edu

Grant No. MRSB-04-006-01-CPPB
Division New England
Term of Grant: 1/1/2004 - 12/31/2006
Total Award: \$ 434,000
Total ACS Support: \$ 434,000

Priority Areas: Cancer Control Survivorship and Outcomes Research 100%

Organ Sites: Breast 100%

Special Categories: Psychosocial and Behavioral, Health Policy or Health Services

Project Summary - Next Page

Grant Profile Information

More than 8 million Americans are alive today who have a history of cancer, and this number is increasing. Unfortunately, surviving cancer usually means enduring significant and prolonged medical treatments that often result in a diminished quality of life. Identification of ways to reduce cancer recurrence and prolong survival, while also improving quality of life, is necessary. From a primary prevention perspective, physical activity has been shown to reduce the risk of breast cancer, and the mechanisms thought to confer this reduced risk may also function in the secondary prevention of cancer. Hypothesized mechanisms associated with primary and secondary risk of breast cancer include an effect of physical activity on metabolic and sex hormones, mammographic breast density, and overall adiposity. To our knowledge, no studies have examined the associations between physical activity and biological mechanisms for breast cancer recurrence in a randomized controlled trial among breast cancer survivors. We hypothesize that an exercise intervention might alter the metabolic and sex hormone profile in breast cancer survivors to one associated with lower risk for recurrence. Further, physical activity has been shown to consistently improve quality of life following cancer diagnosis. The proposed study will test the feasibility of recruiting breast cancer survivors into a six-month randomized controlled moderate-intensity exercise intervention. We will also examine the effect of exercise versus control on biological markers associated with breast cancer and health-related quality of life. We will recruit physically inactive postmenopausal women, ages 40-75 years, with Stage I-IIIa breast cancer, who have completed adjuvant treatment (except for Tamoxifen) and are between one and four years post-diagnosis, from Yale-New Haven Hospital. Breast cancer survivors will be identified using the Rapid Case Ascertainment (RCA) Shared Resource of the Yale Cancer Center. A total of 100 breast cancer survivors will be randomized into one of 2 equal-sized groups: an Exercise Group, and a Control (delayed intervention) group. Baseline and six-month hormone measures, body fat, and quality of life will be assessed and compared. An exercise intervention targeting certain hormones, body fat, and quality of life among breast cancer survivors represents another approach to the problem of long-term cancer recurrence risk, as well as reducing risks associated with other cancers and chronic diseases. Results from such a behavioral intervention could influence the way cancer survivors are managed in the future.

Grant Profile Information

Research Promotion Information

Melinda L. Irwin, Ph.D., M.P.H.

Grant No. MRSB-04-006-01-CPPB

Hometown (currently reside): Westport, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Hartford Courant, Yale Bulletin, New York Times, Connecticut Post, Yale Medicine

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Any volunteer work

Institution Publicity Contact:

Karen Peart

Grant Profile Information

Ming Li, Ph.D.

Function of Phosphatidylserine Receptor in T Cell Development

Yale University
Department of Immunobiology
330 Cedar Street
New Haven, CT 06520
203-7855385 (phone)
203-7371764 (fax)
MINGLI352@YAHOO.COM

Grant No. PF-03-127-01-IJB
Division New England
Term of Grant: 7/1/2003 - 6/30/2006
Total Award: \$ 124,000
Total ACS Support: \$ 124,000

Mentor: Richard A. Flavell, Ph.D.

Priority Areas:	Biology	30%
	Scientific Model Systems	70%
Organ Sites:	Leukemia	20%
	Non-Hodgkin's Lymphoma	80%

Special Categories:

Project Summary

Efficient host defense against pathogen infection and cancer depends on the establishment of a functional immune system where generation of T lymphocytes is a key element. T cells develop in the thymus and carry a myriad collection of surface receptors to meet the specificity of immune responses. T cell receptors are produced stochastically, which can result in nonfunctional or self-reactive T cell clones that are deleted by cell apoptosis. In fact, the selection pressure is so high that more than 97% of T cells are eliminated in the thymus. Dead cells are engulfed by phagocytes, which ensures appropriate T cell development. Molecules involved in the phagocytosis of apoptotic cells have recently begun to be identified and my proposal focuses on one of these molecules, phosphatidylserine receptor (PSR).

To study the *in vivo* function of PSR, I have created a strain of mice deficient in PSR. These mice have defects in various organs including brain, lung and thymus, demonstrating an essential role for PSR in mouse development. Since apoptosis is critically involved in T cell differentiation, I propose to study the thymus phenotype of PSR-deficient mice. To this end, experiments will be designed to further characterize the role of PSR in T cell selection processes; to study the activity of T cells and supporting stromal cells in PSR-deficient mice; to look for the expression pattern of PSR in the thymus; and to study the function of these PSR-expressing cells. It is anticipated that these studies will provide a framework for understanding how phagocytes shape the T cell repertoire, which is essentially involved in adaptive immunity.

Grant Profile Information

Research Promotion Information

Ming Li, Ph.D.

Grant No. PF-03-127-01-LIB

Hometown (currently reside): New Haven, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Richard A Flavell, Ph.D.

Grant Profile Information

Andrew T. Mackey, Ph.D.

Mutational Analysis of the Intestinal Epithelial Brush Border

Yale University
Department of Molecular, Cellular and
Developmental Biology
KBT 342
266 Whitney Avenue
New Haven, CT 06520
203-432-3469 (phone)
203-432-6161 (fax)
andrew.mackey@yale.edu

Grant No. PF-04-244-01-CSM
Division New England
Term of Grant: 12/1/2004 - 8/31/2007
Total Award: \$ 112,500
Total ACS Support: \$ 112,500

Mentor: Mark S. Mooseker, Ph.D.

Priority Areas:	Biology	75%
	Scientific Model Systems	25%
Organ Sites:	Colon - rectum	60%
	Small intestine	40%

Special Categories:

Project Summary - Next Page

Grant Profile Information

Generally speaking, at least one person that each of us knows will develop colon cancer at some point in their life. But we understand little about how the cells of the colon become cancerous. We need a better understanding of the basic unit of cancer, the cell, how it works, what controls keep it from becoming cancer, and what we can do to prevent cancer from occurring. To understand what changes happen to the intestinal cell to make colon cancer occur, I propose to investigate several proteins within the intestinal cell that help to give the intestinal cell its unique appearance and function. Intestinal cells are polarized, meaning that the intestinal cell has clearly defined sides that are different from one another. One side of the intestinal cell faces the inside, or lumen, of the gut, while the other side faces the blood stream. The intestinal cell must maintain its integrity so that the blood stream does not become flooded with the various microorganisms that reside within our gut. I am interested in the proteins that reside at the apical side of the cell, the side that faces the gut. On the apical side of each cell is a surface with hundreds of finger-like projections called microvilli. These microvilli contain the necessary enzymes and transporters to absorb the nutrients and water that we eat and drink. We do not totally understand how the intestinal cell becomes polarized or how the microvilli assemble, but we do know that cancer cells do not have microvilli, because this structure is not necessary for the cancer to grow and spread. Therefore, by systematically altering the microvilli, we may be able to observe some of the transitions that occur when an intestinal cell becomes cancerous. To that end, we have recently generated mutant mice that are missing specific components to the microvilli of intestinal cells. These mice are alive, but exhibit characteristics that are not normal for intestinal cells. The next step of this analysis is to make double-mutant mice for these components and observe the changes in microvilli order and arrangement. This project will hopefully allow us to understand the behavior of intestinal cells and give us some insights about how these intestinal cells become cancerous.

Grant Profile Information

Research Promotion Information

Andrew T. Mackey, Ph.D.

Grant No. PF-04-244-01-CSM

Hometown (currently reside): New Haven, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Karen Peart

Grant Profile Information

Margaret A. Macris, Ph.D.

Role of the RecQ4/RTS Helicase in Genome Maintenance

Yale University
Department of Molecular Biophysics and
Biochemistry
SHM C130
333 Cedar Street
New Haven, CT 06520-8024
203-785-4569 (phone)
203-785-6037 (fax)
margaret.macris@yale.edu

Grant No. PF-05-227-01-GMC
Division New England
Term of Grant: 7/1/2005 - 6/30/2008
Total Award: \$ 138,000
Total ACS Support: \$ 138,000

Mentor: Patrick Sung, Ph.D.

Priority Areas: Biology 100%

Organ Sites: Bone 100%

Special Categories:

Project Summary

DNA, every organism's hereditary material, can be damaged by environmental agents, like radiation, as well as by endogenous (internal) factors. Repair of damaged DNA is critical to the survival of the cell and maintenance of the genome (an organism's entire set of genes). We are interested in understanding the mechanism of homologous recombination (HR), which is a major pathway for the elimination of double-strand breaks (DSBs), which are the most lethal type of DNA damage. Cells that are defective in HR exhibit high levels of genetic change in chromosomal DNA due to their inability to repair broken chromosomes. Genetic changes in DNA are the underlying cause of cancer. Inherited defects in one class of proteins that are important for HR repair, the RecQ helicases, are associated with the cancer-prone human disorders called Bloom's Syndrome, Werner's Syndrome, and Rothmund-Thomson Syndrome (RTS). Patients with RTS exhibit skin and skeletal abnormalities, growth defects, and an increased incidence of cancers, especially osteosarcomas. The majority of RTS patients have defects in the RECQ4 gene, which encodes one of five RecQ helicases in humans. We have isolated this protein and will investigate its biochemical activities to determine its potential role in HR. We will also study the effects of inhibiting its expression on DNA repair and HR in human cells. The results of our studies on RecQ4 will help us to better understand the origin of cancers in patients with RecQ helicase deficiency and may constitute the basis for devising strategies for the diagnosis, prevention, and treatment of cancer.

Grant Profile Information

Research Promotion Information

Margaret A. Macris, Ph.D.

Grant No. PF-05-227-01-GMC

Hometown (currently reside): Guilford, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

New Haven Register

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Grant Profile Information

Haq Nawaz, M.D., M.P.H.

Physician Training Award in Preventive Medicine

Griffin Hospital
Department of Medical Education
130 Division Street
Derby, CT 06418
203-732-1268 (phone)
203-732-7185 (fax)
haqnawaz@pol.net

Grant No. PTAPM-04-081-01-PTAPM
Division New England
Term of Grant: 1/1/2004 - 12/31/2007
Total Award: \$ 300,000
Total ACS Support: \$ 300,000

Priority Areas:	Cancer Control Survivorship and Outcomes Research	34%
	Early Detection Diagnosis and Prognosis	33%
	Prevention	33%

Special Categories:

Project Summary

There is a need for highly trained physicians and researchers who can carry on the fight against cancer in the 21st century. This is possible only if the medical field can attract and train quality physicians in the field of cancer prevention and control. The receipt of this grant from the American Cancer Society will enable Griffin Hospital and the Yale Cancer Center to strengthen an existing four-year combined training program in Internal Medicine and Preventive Medicine by adding a specialized track in cancer prevention and control. This track will create special opportunities for physicians who are pursuing advanced training in cancer. The funding will provide the necessary means to afford tuition at the Yale School of Public Health towards a Masters in Public Health, stipend and research support, funds to attend and participate in conference and training programs related to cancer, and funding to conduct small independent research studies in cancer prevention and control. During this training, residents will rotate through various hospitals, the Yale Cancer Center, various Departments of Public Health, the National Cancer Institute, and other local research institutes. At the end of this training these doctors will likely pursue life-long careers in cancer prevention, control, and treatment. This training will enable us to strengthen the workforce of trained professionals in the field of cancer.

Grant Profile Information

Research Promotion Information

Haq Nawaz, M.D., M.P.H.

Grant No. PTAPM-04-081-01-PTAPM

Hometown (currently reside): Ansonia, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

New Haven Register, Connecticut Post, Waterbury Republican, Valley Gazette

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

William Powanda

Grant Profile Information

Zheng-Yu Peng, Ph.D.

Structural Consequences of Cancer-Derived Mutations in Tumor Suppressor p16

University of Connecticut Health Center
Department of Biochemistry
MC-3305
263 Farmington Avenue
Farmington, CT 06030
(860) 679-2885 (phone)
(860) 679-3408 (fax)
peng@sun.uhc.edu

Grant No. RSG-02-050-01-GMC
Division New England
Term of Grant: 1/1/2002 - 12/31/2005
Total Award: \$ 796,000
Total ACS Support: \$ 796,000

Priority Areas:	Biology	100%
Organ Sites:	Leukemia	20%
	Melanoma	40%
	Pancreas	20%
	Soft tissue sarcoma	20%

Special Categories:

Project Summary

Cancer is characterized by uncontrolled cell proliferation. Recently, an important set of genes was discovered that regulates the mammalian cell cycle and prevents inappropriate cell division. p16 is an example of one of these genes. In some cases, the risk of developing melanoma runs in families, where a mutation in the p16 gene can underlie susceptibility to melanoma. p16 is an important regulator of the cell division cycle: it stops the cell from synthesizing DNA before it divides. If p16 is not working properly, the skin cell does not have this brake on the cell division cycle, and so can go on to proliferate unchecked. At some point this proliferation can be seen as a sudden change in skin growth or the appearance of a mole. In addition to its role in melanoma, mutations and deletions in p16 have been identified in approximately 40% of all human cancers. Thus, p16 is a multiple tumor suppressor. The goal of this study is to understand the molecular mechanisms by which tumor-derived mutations disrupt the structure and function of the p16 protein. We will identify the structural defects induced by tumor-derived mutations and study their functional consequences. We will also investigate the possibilities of restoring the function of mutant p16 proteins by stabilization of the native state. These studies are important for understanding the molecular pathogenesis of cancer and may lead to novel therapeutic strategies.

Grant Profile Information

Research Promotion Information

Zheng-Yu Peng, Ph.D.

Grant No. RSG-02-050-01-GMC

Hometown (currently reside): West Hartford, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

Hartford Courant

Newline, University of Connecticut Health Center

Alumni Office, Carnegie Mellon University

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Patrick Keefe

Grant Profile Information

Warren D. Shlomchik, M.D.

Analysis of Alloimmunity to CML in a Novel Murine Model

Yale University
Department of Internal Medicine
WWW 217
333 Cedar Street
New Haven, CT 06520
203-737-2478 (phone)
928-395-8571 (fax)
warren.shlomchik@yale.edu

Grant No. RSG-03-058-01-I.IB
Division New England
Term of Grant: 1/1/2003 - 12/31/2006
Total Award: \$ 734,000
Total ACS Support: \$ 734,000

Priority Areas: Scientific Model Systems 100%

Organ Sites: Leukemia 100%

Special Categories:

Project Summary

The use of the immune system to fight cancer is a goal of many investigators and has in the past several years received much attention in the popular press. At present, however, so called immunotherapy is only applied as a standard of care in the setting of bone marrow or stem cell transplantation from a related or unrelated donors (called allogeneic stem cell transplantation; alloSCT). In an alloSCT, the patient receives chemotherapy and/or radiation therapy, followed by the infusion of stem cells harvested from blood or bone marrow of a donor. Included in these stem cells are immune cells called T lymphocytes which can recognize the patient as foreign or non-self. This recognition can have both beneficial and harmful effects. In the case of some neoplasms, in particular Chronic Myelogenous Leukemia (CML), these T cells reject the leukemia as foreign. Donor T cells without any chemotherapy can eradicate all detectable CML cells in most patients. Unfortunately, for reasons that are currently unknown, donor T cell therapy is much less effective against many other cancers. Donor T cells can also recognize the non-cancer cells in the patient as foreign, and attack them as well. This effect is the most important obstacle in alloSCT. The goals of the research described in this grant proposal are to: 1) understand why CML is so sensitive to T cell therapy with the long term goal of using this information to develop techniques to make other cancers more sensitive; and 2) to learn how T cell responses against tumor cells and normal cells differ such that we can have the former without the latter. To achieve these goals we propose to study how T cells kill CML cells using a novel mouse model of CML. Of mouse models of leukemia, this one is unique in that it is nearly identical to CML and is caused by the same genetic abnormality. We are optimistic that this research will result in new approaches for immunotherapy that will improve both safety and efficacy.

Grant Profile Information

Research Promotion Information

Warren D. Shlomchik, M.D.

Grant No. RSG-03-058-01-LIB

Hometown (currently reside): Westport, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

New York Times, New Haven Advocate, Fairfield Advocate, Connecticut Post, Hartford Courant,

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Judith Winslow

Grant Profile Information

Hosanna Soler-Vila, Ph.D.

Psychosocial Factors, Race, and Cancer Survival

Yale University
Department of Epidemiology and Public
Health
60 College Street
P.O. Box 208034
New Haven, CT 06520-8034
203-737-2246 (phone)
203-785-6980 (fax)
hosanna.soler@yale.edu

Grant No. MRS GT-05-003-01-CPHPS
Division New England
Term of Grant: 1/1/2005 - 12/31/2009
Total Award: \$ 647,000
Total ACS Support: \$ 647,000

Priority Areas: Cancer Control Survivorship and Outcomes Research 100%

Organ Sites: Breast 25%
Colon - rectum 25%
Endometrium 25%
Prostate 25%

Special Categories: Socio-economically Disadvantaged or Special Populations
Psychosocial and Behavioral, Health Policy or Health Services

Project Summary - Next Page

Grant Profile Information

The overall aim of the proposal is to provide the candidate, Hosanna Soler-Vila, Ph.D., with a supervised training and research experience that will enable her to become an independent investigator focusing on race/ethnic disparities in cancer detection and survival. Dr. Soler-Vila, a social demographer, is currently a post-doctoral fellow at the Yale University School of Medicine being trained in psychosocial epidemiology.

If granted the award, she would undertake relevant substantive and practical training: learning about cancer epidemiology and treatments, behavioral and psychosocial prognostic factors, and advanced biostatistics. The proposed research will investigate psychosocial factors associated with survival among individuals diagnosed with cancer; whether these associations vary by race, age, gender, or stage at diagnosis; and whether completion of treatment explains part of this relationship. The project consists of secondary data analysis of a population-based cohort of African-American and White men and women diagnosed with one of four commonly occurring cancers (breast, colorectal, endometrial, and prostate) in the late 80s; and for whom we have extensive data on socioeconomic, biomedical, and psychosocial factors, together with tumor etiology and treatment information, and 15-year follow-up data on cause-specific mortality and disease-free survival.

Identifying psychosocial factors associated with survival and the potential mechanisms of such associations is a necessary step in designing targeted interventions to reduce mortality and ethnic disparities in cancer survival. The training afforded by this award will enable the candidate to pursue independent research on minority cancer patients with a focus on African-Americans and Hispanics with the ultimate goal of developing culturally-sensitive interventions.

Grant Profile Information

Research Promotion Information

Hosanna Soler-Vila, Ph.D.

Grant No. MRS GT-05-003-01-CPHPS

Hometown (currently reside):

Publications suggested by grantee to receive an ACS grant press release:

New Haven Register, Yale Cancer Center Newsletter, Yale Medical Bulletin

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Renee Gaudette - 203-785-2143

Grant Profile Information

Scott A. Strobel, Ph.D.

Mechanism and Inhibition of Ribosomal Protein Synthesis

Yale University
Molecular Biophysics and Biochemistry
266 Whitney Avenue
P.O. Box 208114
New Haven, CT 06520-8114
203.432.9772 (phone)
203-432-5767 (fax)
strobel@mail.csb.yale.edu

Grant No. RSG-02-052-01-GMC
Division New England
Term of Grant: 1/1/2002 - 12/31/2005
Total Award: \$ 899,000
Total ACS Support: \$ 899,000

Priority Areas:	Biology	90%
	Treatment	10%

Special Categories:

Project Summary

In every organism, the ribosome is the enzyme responsible for converting all the coding information contained within the DNA genome into functional proteins. The machinery of the ribosome is comprised of RNA and protein components, but the evidence is now irrefutable that the RNA is the part of the ribosome that performs the chemical reaction to make protein. This means that every oncogene, transcription factor, digestive enzyme, neural receptor, cell cycle regulator, polymerase, kinase, phosphatase, membrane channel protein, etc. was synthesized within this RNA active site. It is difficult to identify a reaction that is more fundamental to life than translation, yet it remains unclear how the RNA in the ribosome promotes the reaction. These studies will provide a fundamental understanding of translation and the mechanisms of RNA catalysis. Further, the ribosome has commonly served as a therapeutic target, as evidenced by the fact that several naturally occurring and commonly prescribed antibiotics are targeted to the translation machinery; they have also found application as chemotherapeutic agents to treat cancer. This proposal involves the preparation of novel active site inhibitors that are designed to trap the ribosome in an inactive state. Not only will these molecules help elucidate the mechanism of a critical cellular process, but the compounds prepared could lead to improved ribosome inhibitors based upon rational design. These small molecules could be developed as chemotherapeutic agents to treat cancer or as antibiotics to treat secondary bacterial infections in immunocompromised patients.

Grant Profile Information

Research Promotion Information

Scott A. Strobel, Ph.D.

Grant No. RSG-02-052-01-GMC

Hometown (currently reside): Hamden, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

The New Haven Register
Yale Bullentin & Calendar

Grantee willing to dicuss your projects with the media? Yes

Grantee willing to dicuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Larry Haas

Grant Profile Information

Hong Sun, Ph.D.

Using C .Elegans Model System to Dissect PI 3-kinase/PTEN Signaling Pathway

Yale University
Department of Genetics
333 Cedar Street
New Haven, CT 06520
203-737-1923 (phone)
203-785-3418 (fax)
hong.sun@yale.edu

Grant No. RSG-03-246-01-MBC
Division New England
Term of Grant: 7/1/2003 - 6/30/2007
Total Award: \$ 720,000
Total ACS Support: \$ 720,000

Priority Areas:	Etiology	15%
	Scientific Model Systems	85%
Organ Sites:	Brain	40%
	Breast	20%
	Prostate	40%

Special Categories:

Project Summary - Next Page

Grant Profile Information

This application proposes to study a gene that is critically involved in many types of human cancers, most notably prostate and breast cancer. Cancer occurs when aberrant cells in the body begin to grow uncontrollably, then spread to other tissues; eventually they can kill their host. Changes in these cells are triggered by mutations in the genes, the molecular blueprints that direct how cells are built and how they will behave. Some types of genes, called tumor suppressors, function as the guardians of the cells by working to prevent them from turning cancerous. This application proposes to investigate the function of a newly discovered tumor suppressor gene called PTEN. Mutation in the PTEN gene has been found to occur frequently (in 20-30% of cases) in the cells of people with advanced prostate cancer. In addition, the presence of an inherited mutation in the PTEN gene has been found to lead to the development of breast cancer in 30-50% of women with the mutation. These facts suggest a very important role for PTEN in the complex cause-and-effect pathways of the cell which, when disturbed, can cause a normal cell to turn cancerous. We propose to use *C. elegans*, a nematode (or roundworm), to study the chemical chains of events regulated by PTEN. Remarkably, many such pathways in the cell, including the one regulated by PTEN, are so similar in humans and *C. elegans* that one can substitute the *C. elegans* PTEN gene for its human version (or homolog). The advantage of studying *C. elegans* is that it is possible to use a genetic method to identify the molecules involved in a particular process that is, even before we learn about the nuts and bolts of the molecular processes, we can readily detect the consequences of changes in the genes, and use those consequences to figure out the process. This is in contrast to molecular studies, which require that the molecules in question already be known before progress can be made. For example, a nematode with a mutated PTEN will have a certain telltale phenotype, or visibly detectable abnormality in its behavior or morphology. We can then ask which other genes, when mutated, act to reduce or enhance the severity of this phenotype. In the process, we can find novel genes that cooperate with or oppose the action of PTEN. *C. elegans* is widely used as a genetic system for biomedical research. We anticipate that knowledge gained from our studies of the *C. elegans* PTEN pathway will shed light on the complex origins of human cancers, and this may in turn help researchers find better methods of diagnosis and treatment.

Grant Profile Information

Research Promotion Information

Hong Sun, Ph.D.

Grant No. RSG-03-246-01-MBC

Hometown (currently reside): Guilford, Connecticut

Publications suggested by grantee to receive an ACS grant press release:

New Haven Register

New York Times

Grantee willing to discuss your projects with the media? Yes

Grantee willing to discuss to speak at ACS sponsored events? Yes

Grantee willing to serve as an expert or as a member of a speaker's bureau? Yes

Other ways grantee would like to assist ACS:

Institution Publicity Contact:

Karen Peart, Office of Public Affairs