American Cancer Society Awards New Research and Training Grants

Ninety-six grants totaling \$43,808,000 Awarded to 70 institutions nationwide

ATLANTA—October 3, 2012— The American Cancer Society, the largest non-government, not-for-profit funding source of cancer research in the United States, has awarded 96 national research and training grants totaling \$43,808,000 to 70 institutions nationwide in the second of two grants cycles for 2012. Of the grants, 78 are new and 18 are renewals of previous grants. The grants go into effect January 1, 2013.

For more than 65 years, the American Cancer Society has funded research and training of health professionals to investigate the causes, prevention, and early detection of cancer, as well as new treatments, cancer survivorship, and end of life support for patients and their families. Since its founding in 1946, the American Cancer Society's extramural research grants program has devoted more than \$3.8 billion to cancer research and has funded 46 researchers who have gone on to win the Nobel Prize.

Below are highlights of new grants.

- Dr. Connie Lea Arnold at LSU Health Sciences Center in Shreveport, La. will study whether an
 automated system is as effective as a personal phone call as a reminder to complete and return colorectal
 cancer screening kits. Automated calls cost significantly less, use fewer resources, and may be implemented
 in a variety of healthcare settings. But the personal call may better address perceived barriers to screening.
 The two follow-up strategies will be compared to determine both effectiveness in improving screening as
 well as cost effectiveness.
- Jennifer R. Brown, at Dana-Farber Cancer Institute will measure the frequency of known genetic changes in chronic lymphocytic leukemia (CLL), the most common leukemia of adults (and as yet incurable), to see which genetic changes best predict response to treatment in a group with a high-risk form of the disease. The work should significantly advance understanding of high risk CLL and move us closer to selecting specific therapies based on the genetic details of individual tumors, and will serve as a paradigm for personalized medicine in CLL.
- Michelle Fortier of the University of California (Irvine) will investigate mobile technology to improve pain and other symptoms in children with cancer. Her team will develop and implement a mobile tool, called the Pain Buddy, which uses a handheld device to document pain and symptoms that children with cancer experience. The information will be immediately accessible by the treatment team so children can be contacted by the team to address pain and other symptoms. This tool has the potential to improve quality of life in tens of thousands of children undergoing treatment for cancer each year.
- Andrew Grimson of Cornell University will investigate gene expression in healthy and diseased cells, with
 the primary goal to better understand post-transcriptional regulation in humans. His group has developed a
 new technique to efficiently survey large numbers of candidate sequences that could identify the microRNAs
 (miRNAs) in which these sequences are found. This knowledge will be a powerful resource for biologists
 interested in differences in gene regulation between healthy and diseased conditions.
- Hans-Guido Wendel of Memorial Sloan-Kettering Cancer Center will investigate the roots of Follicular lymphoma (FL), the most common form of indolent Non-Hodgkin lymphoma (NHL) with 18,300 new cases per year in the U.S. FL is not curable by chemotherapy, is characterized by continuous relapses and disease progression, and is a cancer Dr. Wendel says has been somewhat neglected scientifically. Dr. Wendel will work to identify genetic changes that drive the progression to cancer in FL. His will test the potential of a novel inhibitor of CDK4, which they've identified as being associated with about half of all FL cases, seeking to establish a new rational therapy to benefit a large proportion of FL patients.
- Bin He at Baylor College of Medicine leads a group that has discovered a novel protein called GATA2 that controls androgen receptor expression and function in prostate cancer cells. While most patients respond to androgen deprivation using surgery or hormones, increased androgen receptor expression can cause the cancer to re-grow and become so-called castration-resistant prostate cancer (CRPC), a terminal disease. Dr. He's team has done studies to suggest inhibiting the GATA2 function can suppress androgen receptor expression and stop the growth of CRPC.
- Hushan Yang at Thomas Jefferson University will test the hypothesis that baseline serum small non-

coding RNAs (sncRNA) expression signatures can predict the long-term risk of developing liver cancer in patients with chronic hepatitis B (CHB), one of the top risk factors for liver cancer in the United States. This study will be conducted in a unique and highly homogenous Asian American CHB patient population with more than 2000 CHB patients that have been followed for up to 23 years. It has the potential to reduce the risk disparity for Asian Americans of developing HCC compared to other ethnic groups in the United States.

- Susumu Kobayashi of Beth Israel Deaconess Medical Center will explore the possibility that modulating a certain family of proteins could be a novel therapeutic approach for myeloproliferative neoplasms (MPNs). The study will rely on a variety of techniques, including genetic and biochemical analyses, cell culture, and genetically engineered mouse models, with the goal of developing new, safer methods of clinical therapies for MPNs, which are characterized by the excess production of one or more lineages of mature blood cells leading to symptoms such as headaches, blurred vision, increased size of spleen and liver, and either blood clots or bleeding. The diseases are related to, and may evolve into certain forms of blood cancers such as acute myeloid leukemia.
- Pamela Kreeger at the University of Wisconsin-Madison is studying how communications between
 ovarian cancer cells and macrophages, a cell type in the immune system, can result in surrounding cells
 inappropriately driving tumor cell growth. Her team will identify proteins that macrophages produce to
 influence tumor cells and test several treatment strategies against the process. The proposal represents one
 of the first applications of bioengineering approaches to the complex problem of identifying effective
 treatments for ovarian cancer.
- Erica Larschan of Brown University aims to understand how DNA "packaging" controls how genes are turned on or off. Her team will use fruit flies to study gene regulation and how proteins involved in opening tightly packed DNA identify particular regions along a single chromosome within a very complex genome. In humans, the proteins involved in DNA packaging are targets for already existing anti-cancer drugs. The types of changes in DNA packaging analyzed in this proposal have been associated with a large number of cancers, from leukemias to breast cancer. The proposed research will provide a strong foundation for discovery of new approaches to modulate gene regulation in human cancers.
- Eduardo Mendez of Fred Hutchinson Cancer Research Center is leading a study that would be the first in humans to characterize the genetic abnormalities associated with head and neck cancer metastasis, or spread to other parts of the body. Patients with head and neck cancer are often not diagnosed until the disease is far advanced. They hope to use the information to identify gene targets whose silencing would render these cells more sensitive to current treatments.
- Larisa Nonn at the University of Illinois, Chicago, will investigate vitamin D's role in affecting a class of molecules called microRNAs that have emerged as master regulators of cell fate, differentiation, and carcinogenesis. Studies in people and animals show that vitamin D may protect against prostate cancer and may have a role in the treatment of prostate cancer. The prevalence of vitamin D deficiency in elderly men, who are at the highest risk for prostate cancer, is 60% and on the rise in the United States. This new proposal will provide in depth insight into the role of microRNA regulation in prostate carcinogenesis and the ability of vitamin D to alter microRNA levels. Furthermore, as microRNA targeted cancer therapies emerge, vitamin D may have use as a complementary agent to enhance efficacy and/or safety of those treatments.
- Matthew Sarkisian at the University of Florida leads a team that has identified a subpopulation of cells in glioblastoma (GB) that extend tiny hairlike structures, called cilia, from the cell, which may explain how these tumors resist current therapies. The cilia function like 'cellular antenna' that sense and respond to changes in the surrounding extracellular environment, promoting cell proliferation and survival of cells in stressful situations, like when exposed to chemotherapy and radiation therapy. Ultimately, they envision new treatment strategies that target cilia, and helping to eliminate cells that survive current therapies and potentially significantly extend or save patient lives.
- Pier Paolo Scaglioni at UT Southwestern Medical Center and team has performed genetic testing to
 identify several genes that when inhibited cause the death of lung cancer cells either by themselves or in
 association with treatment with a certain class of drugs. Their new study will characterize the vulnerabilities
 in those genes in the hopes of supporting development of effective therapies for non-small cell lung cancer
 (NSCLC). They anticipate that this research proposal will lead to the development of novel, genotype
 specific, targeted cancer therapies for this devastating disease.
- Rebecca Schweppe at the University of Colorado Denver will study an emerging molecular target for
 thyroid cancer; a protein called tyrosine kinase Src. The goals of the proposal are to understand the
 regulation and function of the Src pathway in thyroid cancer, and ultimately to identify genes and pathways

that interact with Src for future combination therapies.

- Matthew Dean Shortridge at the University of Washington will study a specific microRNA, microRNA-21, which is abnormally expressed in many cancer cell type. MicroRNAs can silence the expression of proteins that suppress tumor growth and help to keep our cells from growing uncontrollably. Initial evidence strongly suggests that inhibition of microRNA-21 function could be a viable therapeutic strategy. Unfortunately, current methods to reduce the function of microRNA-21 have severe side effects and significant pharmacological problems. The long term goal of this proposal is to establish a new strategy for inhibiting the function of microRNA-21, with the goal of new cancer therapeutics exploiting a completely new mechanism of action.
- Rodney A. Stewart at the University of Utah will focus on metastasis, most often the reason cancer
 patients succumb to cancer, which often occurs years after diagnosis. Understanding the genetic pathways
 that promote metastasis is a critical step in developing therapies to prevent, slow, or kill metastatic cells.
 Recent research efforts have begun to uncover some of the genes responsible for regulating metastasis.
 This proposal will use zebrafish to identify genes required for normal cell development in the embryo and
 determine if these genes are related to known metastasis-promoting genes, in hopes of developing new
 metastasis models that could identify novel drug targets.
- Alexia A. Wright of Dana-Farber Cancer Institute will examine the reasons why chemotherapy is sometimes given very close to death and whether doing so improves patients' quality of life. This team will study a group of patients with ovarian cancer. Patients with incurable ovarian cancer often indicate a preference to stop chemotherapy several months before death, but research suggests that chemotherapy decision-making may be driven by physicians rather than on patient preferences. The results from these studies will provide an evidence base to help patients and physicians more accurately determine whether chemotherapy is likely to improve patients' quality of life and outcomes.
- Shan Zha of the Columbia University Medical Center will investigate how a certain gene mutation leads to defects in DNA repair, which increases the risk for leukemia and lymphomas. The study will also generate mouse models for human lymphoma and leukemia that could be used for developing better diagnosis and treatment for the related human diseases.
- Siyang Zheng of Pennsylvania State University will investigate how metastatic cancer cells release circulating tumor cells (CTCs) that travel through the blood and invade different parts of the body, a process that accounts for over 90% of cancer related deaths. These researchers have taken a novel approach to obtaining CTCs, a challenging process, using an array of flexible microsprings to improve the filtration process. This could allow testing of drugs to measure their benefit without exposing a patient to the unnecessary cost or toxic effects of chemotherapy. Since this technological platform is applicable to almost every type of cancer, it could quickly revolutionize the way that therapies are derived for metastatic cancer patients.

The American Cancer Society's research and training program emphasizes investigator-initiated, peer-reviewed proposals, and has supported groundbreaking research that has led to critical discoveries leading to a better understanding of cancer and cancer treatment. Grant applications are ranked on the basis of merit by one of several discipline-specific Peer Review Committees, each of which includes 12 to 25 scientific advisors or expert reviewers. The Council for Extramural Grants, a committee of senior scientists, recommends funding based on the relative merit of the applications, the amount of available funds, and the Society's objectives. No member of the American Cancer Society's Board of Directors or National Assembly may serve on a Peer Review Committee or as a voting member on the Council for Extramural Grants.

The Council for Extramural Grants also approved 88 research grant applications that could not be funded due to budgetary constraints. These "pay-if" grants represent work that passed the Society's multi-disciplinary review process but go beyond the Society's current funding resources, and which will be funded if additional monies become available. These grants serve as an important reminder that there continues to be promising research that cannot with current resources. For more information about the American Cancer Society Research Program, please visit http://www.cancer.org/research.

To learn more, please see <u>Currently Funded Projects</u> on cancer.org/research.