Hope Funds for Cancer Research

Press Release

Hope Funds for Cancer Research Announces 2012 Postdoctoral Fellows

NEWPORT, RI -- July 5, 2012 -- Hope Funds for Cancer Research, an organization dedicated to advancing research for the most difficult-to-treat cancers, announced today it has selected this year's recipients for its Hope Funds Postdoctoral Fellowships. The Hope Funds Fellowships reflect the organization's strong commitment to promoting scientific innovation.

"We are privileged to have the opportunity to fund these extraordinary young investigators. We believe they will devise new approaches to understanding these very difficult cancers," states Charles V. Baltic III, Chairman of the Program Committee of the the Board of Trustees.

Applications for the fellowships came from the country's most prestigious research institutions and were reviewed by a global scientific study session comprised of key-opinion-leader scientists working in oncology. From more than one hundred applications, the Hope Funds selected its three 2012 grantees: Gina DeNicola, Ph.D., at Beth Israel Deaconess, who is studying cancer metabolism in lung cancers; Simon Knott, Ph.D., at Cold Spring Harbor Laboratory, who is investigating the application of combinatorial techniques to pancreatic cancer; and Thales Papagiannkopoulos, Ph.D., at the David H. Koch Institute for Integrative Cancer Research at MIT, who is working to better understand the influence of circadian rhythms in cancer. Each Fellow will receive $142,500 over three years to fund his or her research.

About the Fellows

Gina DeNicola, Ph.D., Beth Israel Deaconess, in the laboratory of Lewis Cantley, Ph.D.
Lung cancer accounts for the greatest number of cancer-related deaths in the United States due to its high incidence rate and poor response to existing therapy. Alternative strategies such as targeting the altered metabolism of cancer cells may lead to more successful treatment of this disease. It is widely believed that the reactive oxygen by products of cellular metabolism drive cancer progression and promote many tumorcigenic processes; however, Dr. DeNicola has shown that tumor cells actively lower these reactive oxygen species (ROS) to avoid cellular damage and death. She has now found that a key regulator of mitochondrial ROS is required for the survival of lung tumor cells. Dr. DeNicola's work will focus on characterizing the function of this protein and understanding its contribution to cancer development in cell culture systems and mouse tumor models. As this ROS regulator is perturbed in the high percentage of human cancer cases, her work may provide a suitable, and so far unappreciated, therapeutic target for the treatment for these patients.

Simon Knott, Ph.D., Cold Spring Harbor Laboratory, in the laboratory of Gregory Hannon, Ph.D.
Loss-of-function RNAi screens that target tumorgenic genomic factors are a powerful and commonly drawn weapon in the war on cancer. However, using current tools, these screens often produce less than industrial strength results. Dr. Knott's research is aimed at improving the quality and robustness of these tools, thus he does not focus on a specific cancer per se. With that said, the model Dr. Knott has chosen to develop these tools in is Pancreatic Cancer.

RNAi screens, as they pertain to cancer research, are driven by the premise that oncogenic changes alter the dependencies of cells, making them vulnerable to the loss of driving oncogenes and to addictions that the transformed state creates. There are cases where this paradigm has proven successful, like Gleevec, Tarceva and B-RAF inhibitors. However, there are inevitably patients who fail to respond or, more commonly and perhaps predominately, initially respond but later acquire resistance to single-target therapies. The reasons for initial and outright resistance are several-fold. Chief among them is heterogeny in cancer cell populations due to additional mutations acquired between the time of the initial driver mutation and the time of treatment. For example, the chronic myeloid leukemia drug Gleevec, which targets the tyrosine kinase enzyme ABL, is rendered ineffective in patients with additional mutations in the BCR-ABL enzyme. The mechanisms behind delayed and/or acquired resistance appear to be more complex. Cellular pathways are dense, highly connected and adaptable. Following the exposure of cancer cells to a targeted therapy, the pathways involved is typically up- or down-regulated as anticipated. However, having rapid rate of proliferation and anti-apoptotic tendencies, these cells can overcome this initial therapeutic onslaught by taking advantage of pathway plasticity. Up- or down-regulating parallel or related pathways, tumor cells are able to compensate for the loss of targeted gene/pathway. To overcome the shortfalls of single-target therapeutics, it is necessary to turn towards combinatorial agents targeting critical notes of multiple pathways. Dr. Knott's research is building methods to identify high efficacy multi-targeted therapeutics.

Thales Papagiannakopoulos, Ph.D., at the David H. Koch Institute for Integrative Cancer Research at MIT, in the laboratory of Tyler Jacks, Ph.D.
Dr. Papagiannakopoulos' research focuses on lung cancer. Lung cancer is the leading cause of deaths worldwide. The Jacks laboratory has established an autochthonous mouse model of human lung adenoma and adenocarcinoma. In these genetically engineered mice (GEMs), lung tumors are induced in K-ras LSL-G12D/4; p53 flox/flox (KP) or K-ras LSL-G12D/+ (K) mice after inhalation of viral vectors expressing Cre-recombinase, which activate a K-ras G12D allele and concomitantly deletes the tumor suppressor p53 in lung epithelial cells. K and KP tumors mimic human lung tumors in their progression showing similarities both in the molecular and histological levels. Further more, this study will uncover fundamental aspects of lung tumor initiation and progression that will likely extend to many other types of cancer.

It is becoming increasingly clear that in the modern western lifestyle, environmental factors in cooperation with genetic events contribute greatly to the occurrence of cancer. A major consequence of a modern lifestyle is the disruption of circadian rhythms, which are highly conserved daily oscillations that align physiological functions with the day/night cycles. Loss of circadian clock synchrony is associated with the range of diseases, including cancer. Conversely, carcinogenesis could lead to disruption of circadian clock homeostasis, with subsequent defects in all circadian-related functions, such as proliferation and metabolism. Epidemiological studies have revealed that the risk for many types of cancer is significantly higher in industrialized societies, particularly among shift-workers. In 2010, the World Health Organization and the International Agency for Research on Cancer published an assessment on carcinogenicity of shift-work which concluded: "shift-work that involves circadian disruption is probably carcinogenic to humans." This raises many concerns, since the United States alone, it is estimated that 20% of the work force is subjected to shifting work schedules. Dr. Papagiannakopoulos' proposal outlines the different approaches he will utilize to test the importance of circadian rhythm disruption in cancer. This approach will uncover the functional importance and provide molecular insight into circadian rhythm disruption in lung tumor initiation and progression. Finally, this study will provide critical mechanistic insights for the development of circadian rhythm-based therapeutic approaches in cancer.

About the Hope Funds Fellowships
The Hope Funds for Cancer Research supports research for highly innovative projects that challenge the traditional paradigms associated with understanding the causes, mechanisms, progression, disease markers, or risk factors of the most difficult-to-treat cancers. The Hope Funds believes it is important to emphasize creative approaches to research and award grants to young scientists based on the following criteria: project innovation and originality; the significance and direct relevance of the research proposal; the project's approach and conceptual

framework; the researcher's qualifications and those of his or her mentors; and the quality of the researcher's overall working environment. To learn about all Hope Funds Fellows visit: 2012 Fellows, 2011 Fellows, 2010 Fellows, 2009 Fellows, 2008 Fellows

About the Hope Funds for Cancer Research
The Hope Funds for Cancer Research was formed in 2006 by individuals with experience in science, medicine, intellectual property law, investment banking, philanthropy, sociology and the arts, who wanted to establish a funding vehicle that would take a rational scientific, medical and investment approach to awarding research grants. A strong emphasis is placed on identifying innovative and promising research efforts to address the most difficult-to-treat cancers, including pancreatic, lung, liver, sarcomas, esophageal, brain, gastric, ovary cancers, rare leukemias and lymphomas, and MDS. The Trustees of the Hope Funds for Cancer Research believe that funding innovative research that can lead to medical breakthroughs and increased life expectancy is at the core of its mission. The Hope Funds for Cancer Research is a 509(a)(1) charity under 501(c)(3) of the Internal Revenue Service's code. For additional information about the organization, please visit www.hope-funds.org

Hope Funds for Cancer Research is an independent and unaffiliated non-profit organization

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