Cancer Research & Treatment Fund, Inc.

CR&T™

CANCER SURVIVORS HALL OF FAME™

SPRING 2009

CR&T ANNOUNCES GRANTS

Cancer Research & Treatment Fund has awarded grants to four distinguished scientists' specializing in research and treatment:

David Scheinberg, M.D., Ph.D.
Memorial Sloan-Kettering Cancer Center

Dr. Scheinberg is the Chairman, Molecular Pharmacology and Chemistry Program, specializing in developing targeted immunotherapies at Memorial Sloan-Kettering. He also holds the position of Professor of Medicine and Pharmacology at Weill Cornell Medical College.

Research Summary:

The development of anti-cancer agents targeting the mitochondria (the energy producer in cells) that may be effective in treating a broad range of cancers. They have discovered a new mitochondrial based pathway for processing of proteins encoded within the mitochondria of cancer cells. These proteins are all involved in the production of energy for cells. Blocking this pathway appears to selectively kill cancer cells, both in vitro and in animal models. This research seeks to develop better inhibitors of this pathway, which may lead to drug candidates.

Chris Schaffer, Ph.D., Cornell University

Dr. Schaffer received his Ph.D. from Harvard University and is an Assistant Professor at Cornell University in the Department of Biomedical Engineering. His research has centered on the development of optical tools for in vivo manipulation of biological structures and the use of these tools to study the role of cortical microvascular lesions in neurological disease.

Research Summary:

Our study focuses on the effects of polycythemia vera on blood flow in the brain. The elevated hematocrit associated with this disease increases blood viscosity and likely impairs blood flow to the brain. Such decreases in blood flow could lead to injury to brain cells and consequent cognitive decline. We utilize in vivo two-photon excited fluorescence microscopy to measure the speed of blood flow in individual vessels in the brain of transgenic mice that carry the JAK2 mutation that has been associated with polycythemia vera in humans. Our work will provide a detailed understanding of brain circulation in high hematocrit conditions that can be directly translated into understanding cognitive impacts of polycythemia vera and establishing treatment guidelines.

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NEW DEVELOPMENTS IN THE THERAPY OF NON-HODGKIN'S LYMPHOMA

John P. Leonard, M.D.

Richard T. Silver Distinguished Professor of Hematology and Medical Oncology, Center for Lymphoma and Myeloma, Division of Hematology/Oncology, Weill Cornell Medical College and New York-Presbyterian Hospital, New York, New York.

The treatment of non-Hodgkin's lymphoma (NHL) remains a complex clinical problem. A major challenge is the fact that there are over 40 different lymphoma subtypes, and tailoring therapy to individual patient subsets is desired but difficult. With some indolent lymphoma subtypes, cure is not expected but a chronic course is typical. Short of eradicating the disease, having tools that can effectively control the disease for an extended period with minimal toxicity and maintain quality of life is essential. In aggressive lymphoma types, a significant proportion of patients can be cured with chemotherapy-based regimens. However, new approaches are needed to further improve cure rates and to reduce toxicity. At Weill Cornell Medical College, we have undertaken several initiatives with the aim of improving outcomes and quality of life for patients affected by the spectrum of lymphoid cancers.

Lymphoid malignancies represent the first area where the use of monoclonal antibody

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THE 5TH INTERNATIONAL MPD PATIENT SYMPOSIUM

by David Boule, CR&T Board Member

Let's start with the basics—what is a myeloproliferative disease (MPD)?

There are four myeloproliferative diseases which share many clinical characteristics and reflect overactivity of the bone marrow. These are polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF), and chronic myeloid leukemia (CML). CML is split off from the other three because it is characterized by a specific chromosomal abnormality and very specific drug treatment which results in prolonged remission and possibly cure.

DAVID BOULE

The other three clinically related myeloproliferative diseases (MPDs) will be discussed at the Patient Symposium. In these MPDs, the marrow cells that produce blood cells function abnormally and overproduce (proliferate) red blood cells, white blood cells and/or platelets. PV and ET are chronic diseases which generally can be managed over the long term with appropriate treatment. PMF is chronic and develops without any antecedent disorder. Sometimes, a clinically similar picture develops in late stages of PV and ET.

Currently, there is no known cure for any of the MPDs. But significant advances in understanding the MPDs have been made recently with the discovery of a mutated gene (JAK2 V617F) found to be highly associated with the MPDs, especially PV. (Researchers at Cornell have found the JAK gene to be present in virtually all patients with PV). Additionally, alternative treatments have been developed, particularly using low doses of interferon which can reduce or even stop fibrosis of the bone marrow associated with advancement of the diseases. Moreover, there are several clinical trials currently being conducted as a result of the discovery of the JAK2 gene mutation.

The 5th International MPD Patient Symposium

Dr. Richard T. Silver, Vice President and Medical Director of CR&T, has long been recognized worldwide as a leading expert in the diagnosis, treatment and clinical research related to MPDs. Under Dr. Silver's leadership, the CR&T sponsored its first MPD Patient Symposium in 2001. The Patient Symposium immediately preceded the inaugural International Congress on Myeloproliferative Diseases and Myelodysplastic Syndromes for physicians which Dr. Silver also initiated. Dr. Silver recognized the need to provide a forum for MPD patients to come together to learn from both the physicians and clinical researchers who specialize in their disease because these diseases are not widespread (the best estimate is that fewer than 200,000 in the US have one of these three MPDs). As importantly, Dr. Silver recognized the need for the patients to have the opportunity to talk with others about how they cope with their disease.

In 2007, Dr. Silver asked the MPD Foundation, a Chicago based organization to co-sponsor the event and to invite the many MPD patients on its list to attend the symposium in New York City. Like CR&T, the MPD Foundation raises funds and distributes grants to researchers engaged in finding a cure or better treatments for MPDs. In 2009, the MPD Foundation will also co-sponsor the Symposium. This approach allows the Symposium to keep patient ticket prices low and allow access to the broadest possible MPD patient audience.

We expect to have more than 200 patients attend the Symposium on November 4, 2009 at the New York Athletic Club. We're really looking forward to a great MPD patient educational experience. More informed MPD patients can be more effectively involved in their own treatment.

Dr. Silver asked me, as a member of both the CR&T and MPD Foundation Boards and a PV patient, to lead the planning for the Symposium event. I was honored and pleased to accept the chairmanship of an inaugural "MPD Patient Committee" to provide input to the Symposium Agenda that Dr. Silver is constructing in his role as Symposium Chair. I hope, with the assistance of a patient committee, to help produce a very interesting and productive educational program for all who attend this symposium. The Patient Committee includes patients who have PV, ET and PMF. We will meet in April to discuss ways the patient experience at the Symposium can be enhanced. Dr. Silver said "We want to provide the patients with the most valuable and useful day possible". I am also working closely with Mike Wargo, CR&T Vice President of Development and folks from the MPD Foundation to plan and execute the Symposium.

Since its formation in 1968, CR&T has been dedicated to exploring blood cancers as the gateway for the cure for many other cancers. CR&T has focused on finding the most effective ways to bring the lab closer to the patient's bedside in the ongoing search for a cure for cancer. The MPD Patient Symposium, where over 200 patients will get to interact with leading MPD clinicians and physicians from the world's leading institutions, is an important aspect of CR&T's dedication and focus.

SAVE THE DATE

CANCER RESEARCH & TREATMENT FUND
5th International Patient Symposium
for the Myeloproliferative Diseases

November 4, 2009

Registration: 8AM
Program: 9AM – 5PM, Lunch Included
Location: New York Athletic Club,
180 Central Park South, New York City

Co-sponsored by: The MPD Foundation

For more information, Please call CR&T at 212-288-6604

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Y. Lynn Wang, M.D., Ph.D.
Weill Cornell Medical College

Dr. Wang is an Associate Professor of Pathology and Laboratory Medicine, and Director, Molecular Hematopathology Laboratory at Weill Cornell Medical College, New York-Presbyterian Hospital.

Research Summary:
A genetic mutation in the JAK2 gene has recently been identified in patients with polycythemia vera (PV), one of many forms of blood malignancies. This discovery has provided a biomarker for the definitive diagnosis of this disease. However, using JAK2 as a therapeutic target for drug development has met with equivocal results in clinical trials. We suspect that there are other molecules and other molecular pathways besides JAK2 that contribute to the formation of this disease. The goal of this research is to identify these unknown molecules and molecular pathways and determine their specific contribution to the development of PV. Understanding these pathways may provide an understanding of rationale treatments for this illness.

Linda Vahdat, M.D.
Weill Cornell Medical College

Dr. Vahdat is an Associate Professor of Medicine at Weill Cornell Medical College, and Director of the Weill Cornell Breast Cancer Center. Dr. Vahdat is also an Associate Attending Physician of New York-Presbyterian Hospital.

Research Summary:
This grant is used to support several critical initiatives. These include projects trying to understand the basic biology of breast cancer (why do some cancers come back and others don't), how to optimize treatment (targeted drug development) and why side effects occur (particularly peripheral neuropathy from chemotherapy and arthritis-type symptoms from hormonal therapy). Recently, the result of a study trying to understand why tumors recur (come back) was presented at the San Antonio Breast Cancer meeting, the pre-eminent breast cancer conference in the world. This study was funded by a grant from CR&T.

In the trial, *The Effect of Tetrathiomolybdate on Circulating Endothelial Progenitor Cells in Patients with Breast Cancer at High Risk of Recurrence,* we found that by depleting copper from women with a high risk of breast cancer recurrence, we could reduce a cell that we believe is critical for cancer recurrence. Other projects include the basic biology behind the growth and metastases of breast cancer. Survivorship is also an important component of patient care and understanding both short and long term effects of the therapies used to cure patients is critical to our mission. Developing new drugs is also an important component of the program and one that is not possible without ongoing support from CR&T.

NEW DEVELOPMENTS

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treatments was demonstrated to be effective, and now these tools have been applied to many different tumor types. Monoclonal antibodies are immune proteins that are injected intravenously into the bloodstream and which are engineered to bind to tumor cells in a targeted fashion. While some antibodies are designed to elicit an immune response against the tumor or directly induce tumor cell killing, others are rendered radioactive to deliver lethal radiation to the tumor cell while minimizing the damage to normal cells. We have participated in and led trials with a number of monoclonal antibodies, including two agents that have since received FDA [Food and Drug Administration] approval. Rituximab, an antibody which binds to the CD20 protein on tumor cells, is an effective single agent treatment for indolent lymphoma (particularly the follicular subtype), and has clinical activity in virtually all other B-cell malignancies. The precise role of rituximab in various treatment settings is currently being defined, either alone or in combination with other therapies. One major area of investigation includes study into the key mechanisms of action of rituximab, as this information as well as the reasons for resistance can lead to new and improved versions which may be better optimized. We are currently studying a "second generation" version of rituximab in clinical trials with promising early results. Our group was the first to use a "combination antibody" treatment approach in lymphoma, without chemotherapy. Rather than using a cocktail of chemotherapy drugs, our hope is to use a combination of targeted antibodies in order to enhance effectiveness while sparing toxicity. Initial results are quite encouraging. One of our regimens is currently under investigation by the Cancer and Leukemia Group B (CALGB), a cooperative group of the National Cancer Institute, which is studying this approach as an initial treatment for follicular lymphoma that could potentially allow patients to avoid or at least delay having to receive chemotherapy. We are also currently exploring a number of other antibodies as treatment for lymphoma, and our group (including Drs. Morton Coleman, Richard Furman, and Peter Martin) is recognized as a leading center in this area of research.

Lymphoid malignancies represent the first area where the use of monoclonal antibody treatments was demonstrated to be effective

A major translational project led by Dr. Jia Ruan in our group, involves strategies to inhibit angiogenesis, thereby starving lymphomas of their blood supply. It has moved

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NEW DEVELOPMENTS

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into the clinical arena which identified patients most likely to benefit. Based on some initial efforts of Dr. Coleman and colleagues, Dr. Ruan is leading a clinical trial of a novel combination of low-dose oral chemotherapy with new biologic therapies that offer patients less toxicity while having impressive anti-tumor activity.

Mantle cell lymphoma remains a significant clinical problem and is an area of intense clinical and translational research. This uncommon form of lymphoma has historically been associated with an unfavorable prognosis and is treated in an aggressive fashion by many centers. Recent data suggest that advances in management have contributed to a significant improvement in survival for mantle cell patients. Our group has appreciated that some patients can have an indolent, less rapidly growing course of disease. Led by Dr. Peter Martin, we have recently analyzed our outcomes and reported that overall survival of our patients treated in a less aggressive fashion is similar to those of other centers which employ much more toxic chemotherapy approaches. This has caused many groups to re-evaluate their management strategy for this disorder. Additionally, we have recently been the first to report results of observation with deferred treatment in selected MCL patients. In addition to these efforts, we are committed to the development of new treatment approaches, particularly those directed at the key biologic pathways associated with MCL. Several agents, including those which target tumor blood vessels, or those which directly interfere with the cell cycle proteins regulating cell division, are actively being investigated in translational studies. Initial efforts have demonstrated proof of concept, and current plans include efforts to rationally combine new targeted therapeutic drugs.

All of these initiatives remain focused on the unmet needs of lymphoma patients. Clinical and translational research has led to breakthroughs in the development of novel personalized approaches which can more specifically target tumor cells and individual patient subsets while minimizing toxicity. While this work presents many challenges, we are confident that outcomes for patients with non-Hodgkin's lymphoma are likely to improve further in the coming years as a result of these efforts.

Donations to Cancer Research & Treatment Fund

Given the nation's current economic news, volatile stock market, Madoff scandal and major bank losses, we at CR&T want our donors to know that our assets are invested very conservatively. As indicated in our last newsletter, we are pleased to report that we continue to maintain our current and projected research commitments. CR&T pledges to remain efficient and effective and accountable to our donors. More than 80% of every dollar spent goes to research and education. We are grateful for your contributions and for sharing in the common goal of finding a cure.

Cancer Research and Treatment Fund, Inc, is a non-profit group of physicians, nurses, and other medical professionals dedicated to research for the treatment of cancer and other blood diseases. Richard T. Silver, MD FACP founded CR&T in 1968.

Dr. Silver is Professor of Medicine and Director of the Leukemia and Myelproliferative Center at Weill Medical College at Cornell University. He is Attending Physician at New York Presbyterian Hospital/Weill-Cornell Medical Center.

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