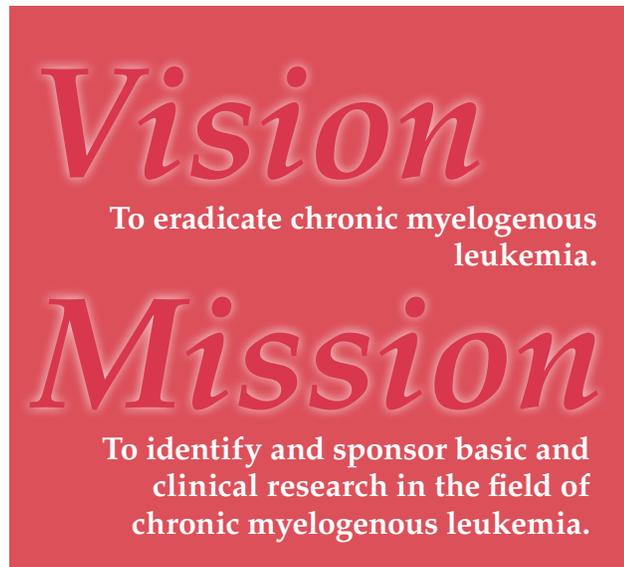


CDMPRP

VII. Chronic Myelogenous Leukemia
Research Program

EXPLORING



Vision
To eradicate chronic myelogenous leukemia.

Mission
To identify and sponsor basic and clinical research in the field of chronic myelogenous leukemia.

The Disease

- ❖ Chronic myelogenous leukemia (CML), also known as chronic granulocytic leukemia or chronic myeloid leukemia, is an overgrowth of granulocytes, a type of white blood cell.
- ❖ In 2007, it is estimated that approximately 4,570 individuals will be diagnosed with CML, and an estimated 490 will die from the disease.¹
- ❖ In most cases, CML is characterized by a chromosomal abnormality that is known as the Philadelphia chromosome.
- ❖ The cause of this disease is unknown but is often attributed to BCR/ABL enzyme activity.
- ❖ CML cells are likely to develop new mutations rendering them insensitive to current treatment options.

Signs and Symptoms

CML is divided into three phases called chronic, accelerated, and acute depending on the stage of the leukemic cells. Symptoms of CML usually develop gradually over time.

- ❖ In the early or chronic stage of CML, there are usually few to no symptoms of leukemia detectable. However, as CML progresses, nonspecific symptoms may become noticeable.
- ❖ Indicators of the accelerated phase include signs such as weakness, fatigue, fever, poor appetite, weight loss, increased sweating, and an enlarged spleen.
- ❖ The acute phase, also called the blast phase, is characterized by significant symptoms that may include weight loss, anemia, fever, bone pain, and recurring infections.

¹ National Cancer Institute Physician Data Query and American Cancer Society, *Cancer Facts and Figures*, 2007.

Program Background

The Department of Defense (DOD) Chronic Myelogenous Leukemia Research Program (CMLRP) was established in fiscal year 2002 (FY02) by Joint Appropriations Conference Committee Report No. 107-350, which provided \$5 million (M) for CML research. The CMLRP has managed **\$22.05M through FY06** to fund peer-reviewed research, and 61 awards have been made through FY06 to eradicate CML (see Figure VII-1, CMLRP Funding History). Over its 5-year tenure, the program has explored answers to basic research questions, encouraged high-risk, high-impact research, and sponsored the development of potential CML-specific therapeutic agents, all in an effort to improve the lives of patients with CML.



CMLRP Making Headlines

- ❖ **Researchers Develop New Strategy for the Treatment of CML**
Virginia Commonwealth University News Release, January 17, 2007
- ❖ **New Weapon to Fight Leukemia**
ScienceDaily, August 27, 2007
- ❖ **Daisies Lead Scientists Down Path to New Leukemia Drug**
University of Rochester Medical Center, October 2, 2007



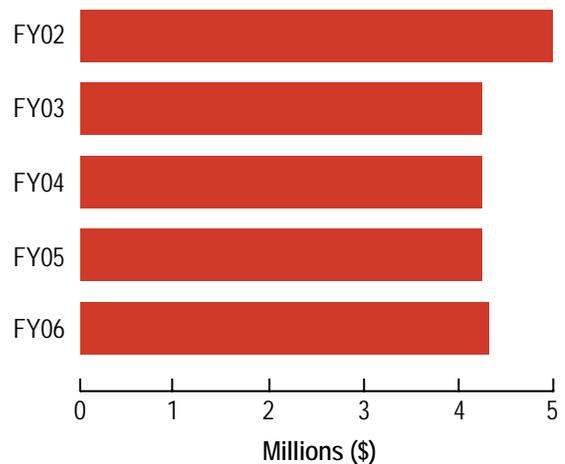


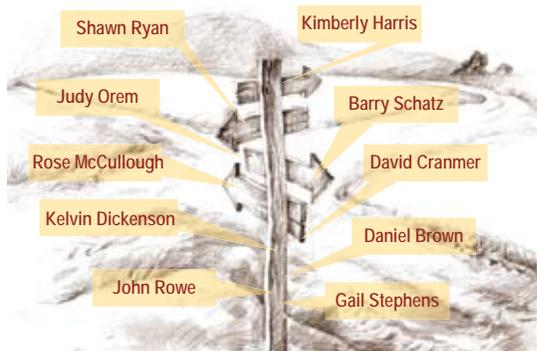
Figure VII-1. CMLRP Funding History

Recognizing Outstanding People

The CMLRP recognizes the importance of assembling intelligent people who understand CML to achieve the vision of the program. Scientists, clinicians, and research managers work collaboratively toward the program’s vision of eradicating CML. The combined efforts of these individuals have greatly contributed to the achievements of the CMLRP.

Consumer Advocates

As active members of the CMLRP, consumer advocates participate in setting program priorities such as guiding the vision for the program and defining cutting-edge investment strategies. CML consumer advocates shape the CMLRP’s research portfolio by partnering with scientists and clinicians in the review of proposals and funding recommendations. **Ten consumer advocates** have served on CMLRP peer and programmatic review panels since the program’s inception in 2002. Consumer advocates’ firsthand experiences with CML provide a unique perspective that is complementary and at times enlightening to the scientific expertise of the panels. This perspective helps scientists understand the human side of how research will impact the community and allows for funding decisions that reflect the concerns and needs of patients, the clinicians who treat them, and survivors and their families. An additional benefit is that consumer advocates take what they have learned back to their communities. As a result of this collaboration, there is an increased awareness of the importance of research and a stronger relationship between the scientific and the consumer advocacy communities. More information about consumer involvement can be found in Section I, Overview.

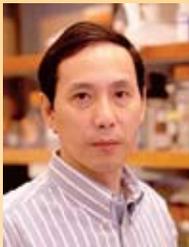


Barry Schatz
FY06 Consumer Peer Review
Panel Member

At the 2006 Road to a Cure meeting, Barry dedicated the moment of silence to all those whose loved ones have been diagnosed with CML. He also revealed how difficult it was for him to explain his own diagnosis to his young sons, and he reflected on how the presence of this life-threatening disease has dramatically changed his perspective of the world. It has also significantly altered the worlds of those closest to him. “It is really only those who have been through this process who can appreciate how deep and far-reaching this impact is, communicate it, and help others undergoing similar experiences.”

Peer Review Panel Members

The CMLRP peer review panels are composed of respected CML-focused scientists and clinicians and dedicated consumer advocates who provide unbiased, expert advice on the scientific and technical merit of the proposals. Peer reviewers also evaluate the overall relevance of the proposals based on the review criteria published for each award mechanism. Scientific reviewers for peer review are selected for their subject matter expertise. Consumer reviewers are nominated by an advocacy or support organization and are selected on the basis of their leadership skills, commitment to advocacy, and interest in science. Approximately **60 scientists, clinicians, and consumer advocates** have participated in peer review for the CMLRP. For additional details about peer review, refer to Section I, Overview.



**Shaoguang Li, M.D., Ph.D.,
Jackson Laboratory
FY06 Peer Review Panel
Member**

“We focus on understanding the molecular basis of human CML. Serving on the CMLRP peer review panel, I reviewed many good grants from leading CML research laboratories. The review process was efficient and fair, allowing for the selection of high-quality and competitive grants for funding. I was also a recipient of the DOD hypothesis grant 2 years ago, and this grant came at a critical time in my scientific career. It provided me with an opportunity to quickly move into the research field of cancer stem cells, leading to our identification of CML stem cells in mice. Attending the Road to a Cure meeting in December of 2006 helped me to meet many experts in the CML field and establish a foundation for further communication and collaboration.”



**Shawn Ryan
FY05 Consumer Peer Review
Panel Member**

“Before you face a life-changing illness, medical research and funding [are just] more of the amorphous background noise of life. Then, when you find yourself dealing with a disease, any bit of information about medical research feels like a life ring thrown to a drowning man...” Shawn, working alongside CML researchers and scientists in peer review, says that his participation brought him one of the most profound experiences he’d had since his diagnosis: “I was blown away by the number and wide scope of the research proposals. I was profoundly struck by the caliber of people dedicated to finding a cure for CML. I walked away feeling that with this kind of brain-power and support working for a cure, it is, seriously, only a matter of time.”

Integration Panel Members

The CMLRP Integration Panel (IP) is composed of prominent and respected scientists, outstanding clinicians, and dedicated consumer advocates. Members of the panel recommend the annual program vision statement and suggest a means to accomplish that vision through the program’s mission statement. Panel members also recommend investment strategies that meet the needs of the research and consumer communities by filling basic science, translational research, and therapeutic development gaps. Individual panel members review proposals and recommend the most programmatically relevant studies for funding (for more information about the functions of the IP, refer to Section I). The CMLRP wishes to extend its deep appreciation to each past and current IP member for their contribution and dedication to the program.



**Ravi Bhatia, M.D., City of Hope
National Medical Center
FY06 Integration Panel Chair**

“The CDMRP has played a critical role in supporting translational and basic research in CML by encouraging researchers to study this disease and by facilitating studies that would not otherwise have been feasible. I have been involved with the review process from the outset, most recently as the chair of the CMLRP, and have been very impressed by the quality and value of the research that has been both stimulated and supported by this program. The value of the program was especially apparent at the recent symposium at which grant awardees reported on their progress. These have been exciting years that have witnessed huge advances in the treatment and understanding of CML, and this program has been at the center of several of these advances.”



**Louis J. DeGennaro, Ph.D., The
Leukemia and Lymphoma
Society
FY06 Integration Panel
Member**

“As a member of an organization whose mission is curing the blood cancers, it has been a special honor to participate in the CMLRP as a member of the Integration Panel. Targeted therapies recently developed to treat chronic myeloid leukemia are on the cutting edge and are showing promise in the treatment of other cancers as well. Continued research on CML, supported by the CMLRP, will help lead the way to the next generation of such therapies.”

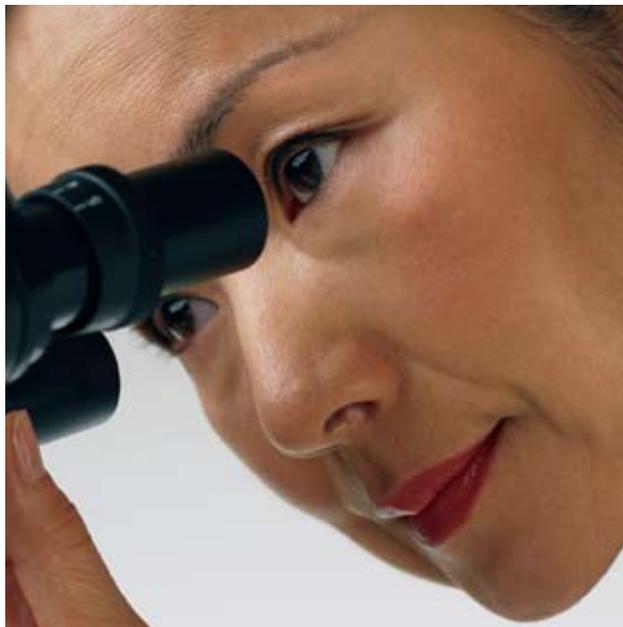
CMLRP IP Members

Name	Affiliation	Years of Service
Current Members		
Ravi Bhatia, M.D. (Chair)	City of Hope National Medical Center	FY06
Jerald P. Radich, M.D. (Chair Emeritus)	Fred Hutchinson Cancer Research Center	FY05–FY06
Louis J. DeGennaro, Ph.D.	The Leukemia and Lymphoma Society	FY06
Kelvin J. Dickenson	The Leukemia and Lymphoma Society	FY06
Alan J. Kinniburgh, Ph.D.	National Hemophilia Foundation	FY02–FY06
Gwen Nichols, M.D.	Columbia University Medical Center	FY06
Ruibao Ren, M.D., Ph.D.	Brandeis University	FY06
Past Members		
Alan J. Gewirtz, M.D.	University of Pennsylvania School of Medicine	FY02
Stephanie Lee, M.D., M.P.H.	Dana-Farber Cancer Institute	FY02
Rose McCullough, Ph.D.	Health Policy Professional	FY02–FY05
Thomas Roberts, Ph.D.	Dana-Farber Cancer Institute	FY02
Janet Rowley, M.D.	University of Chicago Medical Center	FY02–FY04
Anna Schwartz, Ph.D., F.N.P.	University of Washington	FY02
Moshe Talpaz, M.D.	University of Texas M.D. Anderson Cancer Center	FY02–FY05
Richard A. Van Etten, M.D., Ph.D.	Tufts-New England Medical Center	FY03–06



**Ruibao Ren, M.D., Ph.D., Brandeis University
FY06 Integration Panel Member**

“Studies of CML have provided a valuable paradigm for defining molecular mechanisms of cancer, for developing targeted therapies, and for identifying modes of drug resistance. Continued research efforts are critical for progressing the road to a cure. The Department of Defense Chronic Myelogenous Leukemia Research Program has done a great job in using limited funds to push the field forward. Its founding mechanisms and specialized meeting are truly unique and filled many voids of conventional organizations.”



Scientific Community

Exploration of the underlying mechanisms of CML initiation and progression and the development of new therapeutic measures require a concerted effort by the scientific community. A total of 57 investigators have been supported by the CMLRP. The research follows a road from the very basic signal transduction pathways through to the development of newly identified agents for therapeutic use. The CMLRP has funded investigators who are new to the field of CML and investigators who are well established in the field. Highlights of progress from CMLRP-supported investigators follow.

Exploring—Q & A

Q. What signal transduction pathways are most important?

A. Most CML cells carry a chromosomal translocation that creates unregulated BCR/ABL enzyme activity often connected with initiation and progression of CML. In CML patients, BCR/ABL kinase activity may be inhibited by therapeutic options such as imatinib mesylate and dasatinib. However, the CML stem cell population, which may play a role in disease recurrence, is not sensitive to these treatment options, and many CML patients develop resistance to them. Protein phosphatase 2A (PP2A), a protein that exercises a critical role in cell growth, survival, and differentiation, is reportedly progressively downregulated in BCR/ABL-expressing myeloid progenitors undergoing blastic transformation. Dr. Danilo Perrotti hypothesized that inhibition of PP2A activity through increased BCR/ABL kinase activity in CML leukemia-initiating cells plays an important role in maintenance and progression of disease. He used FTY720, a known immunomodulator and inhibitor of PP2A, to study the effects of increasing PP2A activity in BCR/ABL-positive CML blast crisis (CML-BC) cells. Not only did the data demonstrate that FTY720 inhibited BCR/ABL leading to the suppression of CML-BC cell growth, but it also showed that this agent inhibited the growth of BCR-ABL-positive CML cells that are imatinib mesylate and dasatinib resistant. These results indicate that the loss of PP2A activity in CML stem cells may be critical to the development and recurrence of CML.

CMLRP-funded investigators are exploring and defining pathways that play a significant role in the development and progression of CML.



**Danilo Perrotti, M.D., Ph.D.,
The Ohio State University
FY02 Investigator-Initiated
Research Award Recipient
FY06 New Investigator Award
Recipient
FY03, FY04, and FY05 Peer
Review Panel Member**

“I believe that the CMLRP helped me in developing my career as an investigator in the CML field. I do not have doubts that being a CMLRP grantee greatly exposed me to the CML community. Furthermore, the support of the CMLRP certainly facilitated the ... establishment of new collaborations.”

Q. What are the unique characteristics of leukemic stem cells?

A. Under normal circumstances, hematopoietic stem cells give rise to differentiated cells of the blood system. However, CML may develop from dysregulated stem cells that have been shown to be resistant to current therapeutic agents. The persistence of CML stem cells (CML-SCs) may play a role in recurrence of disease and represent a potential target for new therapeutic strategies. Dr. Craig Jordan evaluated the role of NF- κ B, which is upregulated in leukemic cells, in CML-SCs and the conditions for inducing CML-SC-specific apoptosis. Dr. Jordan and his collaborators, addressing the role of NF- κ B in the development of CML-SCs, focused on the expression of eukaryotic translation initiation factor 4E (eIF4E), an NF- κ B-regulated protein. Cellular levels of eIF4E affect the level of nucleocytoplasmic mRNA transport, and activation of NF- κ B leads to increased eIF4E activity. Dr. Jordan's research demonstrated that elevated eIF4E expression levels were associated with suppressed differentiation of granulocytes and monocytes. Further studies determined that increased eIF4E levels caused a cascade of events leading to an increase in the transport of eIF4E-dependent mRNA molecules, including transcripts for cyclin D, known to play an important role in the cell cycle. Analysis of primary CML cells demonstrated that the subcellular distribution of proteins such as cyclin D differed between primary leukemic and non-leukemic cells. Dr. Jordan and his colleagues used I κ B, a repressor of NF- κ B, to suppress NF- κ B activity in cells. The subsequent reduction in NF- κ B activity correlated with reduced expression of eIF4E and a decrease in eIF4E-dependent transcript transport suggesting that eIF4E-dependent mRNA transport may play a role in the development of cancer cells through its ability to affect cell growth and differentiation.

Exploring the molecular characteristics of leukemic stem cells has been funded by the CMLRP and may lead to the development of new therapeutic strategies.



Craig Jordan, Ph.D., University of Rochester
FY02 Investigator-Initiated Research Award Recipient
FY04 Exploration-Hypothesis Development Award Recipient

“Funding from the CMLRP program came at a critical time in my career and provided the support we needed to help advance an exciting new therapy for CML.”

Q. Do currently available animal models accurately simulate human disease?

A. Appropriate models of human disease are valuable tools used in understanding the mechanisms of disease initiation and progression as well as the development of effective therapeutic measures. The challenge for animal model development is the creation of models that mimic disease initiation or progression or respond to therapy in a manner that translates to the clinic. **Through the Exploration–Hypothesis Development Award mechanism, the CMLRP has funded the early establishment of both murine and zebrafish models of CML that may be used for studying mechanisms of disease initiation and progression and the development of new therapeutic agents.**

- ❖ Ricardo Feldman, Ph.D., University of Maryland, proposed the development of a murine model of CML with hematopoietic-specific expression of BCR/ABL that would aid the identification of leukemia-causing genes.
- ❖ Kevin Griffin, Ph.D., University of California, Los Angeles, generated a zebrafish model that expresses the human BCR/ABL enzyme. These fish may be used to identify genetic mutations involved in the development of leukemia as well as evaluate potential new therapeutic agents.
- ❖ Karl Hsu, M.D., Dana-Farber Cancer Institute, developed a vector system to establish transgenic zebrafish that conditionally overexpress BCR/ABL specifically in myeloid stem and progenitor cells to avoid an early lethal BCR/ABL phenotype. Once completed, this zebrafish model may be used to evaluate small-molecule inhibitors of CML.
- ❖ Craig Jordan, Ph.D., University of Rochester, developed a murine model combining the expression of the BCR/ABL kinase with a loss-of-function mutation that develops robust lymphoid blast crisis. This mouse model will be used to evaluate the sensitivity of leukemic stem cell populations to potential CML therapeutic agents.



Q. What is the next-generation therapeutic?

A. Every year an estimated 4,000 to 5,000 persons are diagnosed with CML. The mechanisms for initiation and progression of CML have not yet been clearly defined. However, it is believed that activity of the BCR-ABL enzyme, created from a genetic translocation, plays an important part in both of these processes. The standard of care for CML patients is imatinib mesylate, which blocks the activity of the BCR-ABL enzyme. CML progression involves a slow sequence through three stages of disease (chronic, accelerated, and blast crisis), and treatment options vary with the stage of disease. BCR-ABL-positive CML patients receive treatment with imatinib mesylate followed by dasatinib if resistance occurs. Other treatment options include interferon alpha and bone marrow transplant if a suitable donor is identified.

With all of these treatment options available, one might wonder why scientists still are seeking to develop new CML therapeutic agents. Inhibitors of BCR-ABL activity may be the first line of defense for the management of CML, but not all patients qualify for treatment; some patients do not respond to treatment and others may develop genetic mutations rendering treatment ineffective.

Through the Therapeutic Development Award mechanism, which was designed to sponsor the preclinical assessment of novel therapeutics for CML, the CMLRP funded five proposals that represent a wide range of potential therapies for the future (as described below and illustrated in the time line on the following page).

- ❖ **Histone Deacetylase (HDAC) Inhibitors:** Chaperone proteins, such as heat shock proteins (HSP), play an important role in the process of protein expression by cells. At Medical College of Georgia Cancer Center, the laboratory of Kapil Bhalla, M.D., is studying HDAC inhibitors as therapeutic agents for downregulating the expression of HSP90 function, a chaperone protein that is critical for the expression of the BCR-ABL protein. Primary CML cell populations treated with HDAC6 express lower levels of BCR-ABL in both imatinib mesylate-sensitive and -resistant cells. Suppressed BCR-ABL expression eventually leads to cell death.
- ❖ **Gene Transcription Inhibitors:** Joel Gottesfeld, Ph.D., and colleagues at The Scripps Research Institute have been studying pyrrole-imidazole (Py-Im) polyamide molecules. Dr. Gottesfeld's group has identified specific Py-Im polyamide molecules, 1R-Chl and 8R-Chl, which are capable of inhibiting gene transcription thereby reducing cell growth and proliferation. These compounds do not directly affect enzyme activity and therefore may be useful in treating CML cells that do not express BCR-ABL or that develop resistance to current therapeutic options.
- ❖ **Inosine Monophosphate Dehydrogenase (IMPDH) Inhibitors:** Tiazofurin therapy inhibits the activity of IMPDH, an important factor involved in cell differentiation, and leads to the development of mature, nonproliferating CML cells. However, this treatment compound is rapidly metabolized in the body and becomes inactive. Krzysztof Pankiewicz, Ph.D., at the University of Minnesota, is using a molecular modeling approach to design and develop stable forms of IMPDH inhibitors that may

also have low toxicity. Dr. Pankiewicz and his colleagues have identified and synthesized several candidate structures. Characterization of these compounds in K562 cells, a human erythroleukemia cell line derived from a CML patient, demonstrated that these agents are potent inducers of differentiation. Further in vitro and in vivo studies of these IMPDH-specific inhibitors are planned.

- ❖ **BCR-ABL Inhibitors:** One BCR-ABL mutation that is particularly resistant to TK inhibitor treatment is the T315I mutation. At Temple University, E. Premkumar Reddy, Ph.D., has begun to characterize the activity of a class of compounds that may inhibit the growth of BCR-ABL-positive cells with the T315I mutation. Dr. Reddy and his colleagues have focused on three newly derived compounds that are inhibitors of BCR-ABL activity (ON044580, ON045000, and ON96030) and plan in vitro and in vivo experiments that will establish the mechanism of action and preclinical efficacy of these as future CML treatment agents.
- ❖ **Suppression of Reactive Oxygen Species (ROS)-Induced BCR-ABL Mutations:** Tomasz Skorski, M.D., Ph.D., of Temple University, is interested in preventing molecular events that cause genetic mutations in BCR-ABL. It is known that ROS may damage DNA through the introduction of a variety of oxidized DNA lesions. Dr. Skorski's group has shown that BCR-ABL protein induces the production of ROS and enhances oxidative DNA damage. Data generated from studies of mice fed an antioxidant-rich diet demonstrated a lower frequency of BCR-ABL-associated mutations, and inhibiting ROS decreased the rate of mutagenesis and the frequency of imatinib mesylate resistance in cultured CML cells. Through studying the mechanism of ROS-induced mutations and the susceptibility of specific sequences to this process, Dr. Skorski and his colleagues hope to identify useful therapeutic compounds for decreasing the rate of ROS-induced BCR-ABL mutations thereby increasing the effectiveness of the currently available treatment agents.

1995

- interferon alpha 2a



2006

- dasatinib



- bone marrow transplant

2001

- imatinib mesylate

2007

- nilotinib

The CDMRP is exploring the next generation of treatment options.

- HDAC inhibitors?
- Gene transcription inhibitors?
- IMPDH inhibitors?
- New BCR-ABL activity inhibitors?
- Suppressors of ROS-induced BCR-ABL mutations?

Exploring New Avenues for Research and Collaboration

Road to a CURE

The Chronic Myelogenous Leukemia Research Program

Investigators Meeting

progression of CML for over 30 years, presented a talk entitled “CML: What Questions Remain?” The questions he posed to participants included: Why does translocation occur? What signal transduction pathways are most important? Why do additional mutations of the Philadelphia chromosome occur? What are the unique characteristics of leukemic stem cells? Do currently available animal models accurately simulate human disease? What is the next-generation therapeutic? Many of these questions are being addressed by CMLRP-funded investigators.

The CMLRP sponsored its first research conference, “Road to a Cure: The CMLRP Investigators Meeting,” in December 2006. The meeting was held in Orlando, Florida, and was attended by approximately 50 scientists, clinicians, consumer advocates, and research managers. The meeting provided a forum for CMLRP-funded investigators and consumer advocates to share ideas, forge collaborations, and pursue promising new directions in CML research. Dr. John Goldman, Emeritus Professor of Haematology at Imperial College London, gave the keynote address. Dr. Goldman, who has been involved in exploring the development and



**Joaquin M. Espinosa, Ph.D.,
University of Colorado at
Boulder
Road to a Cure, 2006 Attendee
FY05 Exploration–Hypothesis
Development Award Recipient**

“Being a bit of an outsider to the CML field, the Road to a Cure meeting provided me with a unique opportunity to interact with scientists whose focus is 100 percent on CML. This type of multidisciplinary encounter is very stimulating. After the meeting, my interest in CML and blood cancers in general was solidified, and I am currently writing a collaborative proposal with two experts in hematological malignancies. This proposal is a natural continuation of the research funded by the CMLRP. It is safe to conclude that the Exploration–Hypothesis Development Award and the Road to a Cure meeting played a seminal role in my scientific career by steering some of my research interests into a new direction. I am grateful for the CMLRP’s support.”

CMLRP-funded investigators presented their research findings in one of four General Sessions: models of disease, general basic science, disease characterization, and translational research. The response to the meeting was overwhelmingly positive as 100 percent of the respondents to a post-meeting survey recommended that the Road to a Cure meeting be held again within the next 2 years. CMLRP investigators were able to disseminate research accomplishments; open the lines of communication among the scientific, advocacy, and research administration communities; and explore future collaborations.



**Joel M. Gottesfeld, Ph.D., The Scripps Research Institute
Road to a Cure, 2006 Attendee
FY04 Therapeutic Development
Award Recipient
FY05 and FY06 Peer Review
Panel Member**

Through participation at the Road to a Cure meeting, Dr. Gottesfeld was put in touch with a leading CML investigator. They will collaborate in the testing of molecules developed by Dr. Gottesfeld in primary CML cells and in BCR-ABL transformed cells.



**Krzysztof Pankiewicz, Ph.D.,
University of Minnesota
Road to a Cure, 2006 Attendee
FY04 Therapeutic
Development Award
Recipient
FY05 and FY06 Peer Review
Panel Member**

“The Road to a Cure meeting benefited my research program significantly. Not only could I compare my approach with numerous spectacular advances made by other PIs, but I also found two researchers willing to collaborate with me. Dr. Ruibao Ren of Brandeis University [who] developed a modern and exact mouse model of CML agreed to test some of our anti-CML agents. Dr. Tomasz Skorski of Temple University encouraged me to design some compounds for his studies of the mechanisms regulating DNA repair in leukemias that are related to oxidative stress.”

The Program Today

Fiscal Year 2006 Summary

Congress appropriated **\$4.3M in FY06** to continue the CMLRP. The program offered two award mechanisms to encourage innovation and discovery in the field of CML. A total of **63 proposals** were received across the **two award mechanisms** and **14 awards** were made, as shown in Table VII-1. The Exploration–Hypothesis Development Awards supported untested, groundbreaking concepts in CML research while the New Investigator Awards funded discoveries in clinical translational research. The portfolio developed by the FY06 CMLRP reflects the program’s commitment to both basic and clinically oriented research as reflected in Figure

VII-2. Although Congress did not appropriate funds for FY07, the program continued to actively manage awards funded in previous years that are open for the next several years. Appendix B, Table B-6, summarizes the congressional appropriations and investment strategy executed by the CMLRP for FY06.

The program continues to support previously funded researchers by monitoring progress and capturing the novel and pioneering findings. The CMLRP continues to evaluate the program and update the CMLRP website with research highlights and consumer profiles.

Table VII-1. Funding Summary for the FY06 CMLRP

Categories and Award Mechanisms	Proposals Received	Awards	Investment
<i>Innovative Research</i>			
Exploration–Hypothesis Development	49	11	\$1.7M
New Investigator	14	3	\$2.1M
TOTAL	63	14	\$3.8M

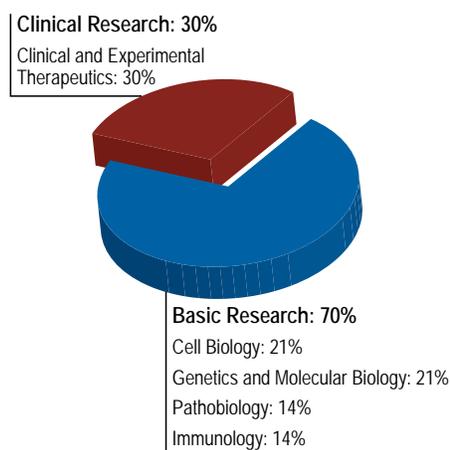


Figure VII-2. FY06 CMLRP Portfolio by Research Area