

PROGRESS REPORT: A YEAR OF RESEARCH INNOVATIONS



From left: Dr. Joseph Scandura, Dr. Shahin Rafii, and Dr. Richard Silver

Throughout the past year, CR&T and its friends have contributed to important advances in research, especially through our support of the Richard T. Silver MD Myeloproliferative Neoplasm (MPN) Center at Weill Cornell Medical College in New York City. Here, talented investigators are conducting basic and clinical studies that will change the face of blood cancer treatment.

“I believe that our purpose is to function as a thought center, bringing experts with diverse expertise together so that they can work to solve complex problems,” says Dr. Joseph Scandura, the Silver Center’s scientific director. In accordance with this philosophy, the Center has launched exciting research collaborations between MPN specialists and Weill Cornell experts in related fields, including:

- **Identifying the “Achilles’ Heel” of MPN Stem Cells:** This study aims to identify the specific genes that MPN stem cells need in order to function. Next, researchers will develop treatments that block these “bad” genes, thereby preventing the production of MPN stem cells.

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While these targeted drugs would eradicate MPNs, they would not interfere with the function of normal stem cells.

- **Leveling the Competition between MPN Cells and Normal Blood-Forming Cells:** A protein called transforming growth factor beta (TGF- β) plays a key role in the production of many types of cells. We already know that MPN patients have abnormally high levels of TGF- β . This study tests the hypothesis that TGF- β causes abnormal MPN stem cells to take over the bone marrow. This dysfunctional process displaces stem cells that stimulate normal blood cell production. If this study is successful, it could lead to new treatments that inhibit TGF- β and that can be combined with other therapies to control or cure MPNs.
- **Pulmonary Artery Hypertension (PAH) in the MPNs:** Little is known about why and how some people with MPNs develop PAH, a cardiovascular complication that can lead to heart failure. To study

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this issue, Dr. Scandura has assembled a consortium of investigators from Weill Cornell and Memorial Sloan Kettering Cancer Center. After examining the echocardiograms of 210 MPN patients, the researchers found that nearly 60 percent had PAH. As part of an extensive study of the relationship between these diseases, the consortium is developing new animal models to help identify the causes of PAH in MPN patients, and to aid in developing new therapies.

- **MPN Avatars to Quickly Test New Therapies:**

Using sophisticated new technologies, Silver Center researchers are implanting tiny portions of human MPN cells into mice. These mouse “avatars” of disease allow investigators to quickly and efficiently test how a particular patient will respond to MPN medications, or to combinations of therapies. A highly innovative research tool, mouse avatars can be used to accelerate the progress of trials of potential new therapies, or to help physicians determine which existing treatments would work best for specific patients.

Mouse “avatars” of disease allow investigators to quickly and efficiently test how a particular patient will respond to MPN treatments.

- **Autologous Cure of MPNs:**

The Silver Center team has developed an exciting new technique that allows scientists to quickly create new hematopoietic stem cells – stem cells that produce all kinds of blood cells – from endothelial cells, which line the interior of blood vessels. This project will use the endothelial cells of MPN patients to make genetically normal hematopoietic stem cells. The next step would be to replace an MPN patient’s existing hematopoietic system with the converted blood cells, which would not carry the MPN mutation—thereby curing the disease.

- **Inflammatory Bowel Disease in MPN Patients:**

Some MPN patients develop inflammatory bowel disease (IBD), which causes inflammation of the GI tract. Conversely, IBD patients often have abnormal blood counts. Previous research showed that 4 out of 23 IBD patients with elevated blood counts also carried an MPN mutation. Now, a collaborative team is exploring the association between the two diseases.

- **Understanding Different Disease Phenotypes of JAK2 MPNs:**

The discovery of the genetic mutation known as JAK2V617F has led to important new MPN treatments. This mutation is found in significant numbers of patients with polycythemia vera and essential thrombocythemia. However, since the two diseases

have different clinical characteristics, it is clear that additional factors are at play. Using state-of-the-art genome sequencing technologies, this study seeks to identify the molecular and cellular processes that account for these differences. Understanding the underlying causes of each disease will help researchers develop new, targeted therapies.

Silver Center researchers are also involved in clinical trials that focus on blood cancer treatment. One notable example is the LAST (“Life After Stopping Tyrosine Kinase Inhibitors”) trial, a national, multi-center study funded by the National Institutes of Health. Dr. Richard

T. Silver, CR&T’s vice president and medical director, conducted early clinical trials of imatinib, the first tyrosine kinase inhibitor (TKI) to receive FDA approval for the treatment of chronic myeloid leukemia (CML). These drugs have been extremely successful in treating this life-threatening disease. However, TKIs can have significant side effects and are very expensive. Therefore, a group of investigators, initially led by a French research team, thought of discontinuing TKIs in patients who had an excellent re-

sponse to treatment.

Building upon this work, the goal of the LAST study is to improve decision making for stopping TKI treatment. To date, approximately 40 percent of patients who discontinued TKIs remain in remission – a figure consistent with the European study results.

To learn more about current clinical trials, please visit the Joint Clinical Trial Office’s website at <http://jcto.weill.cornell.edu>.

Publications

Silver Center investigators have published their findings in key peer-reviewed scientific journals, including *Blood*, *Cancer Cell*, and *Clinical Cancer Research*. Of particular note, Dr. Shahin Rafii, a member of CR&T’s Medical Advisory Board, Dr. Scandura, and other Silver Center researchers published a paper on creating new hematopoietic stem cells in the May 17, 2017 issue of *Nature*.

This is just a sampling of the many exciting research initiatives that you – our donors and friends – are making possible. We will continue to keep you up-to-date in future issues of *CR&T News!*

MESSAGE FROM THE PRESIDENT



Woven into the pages of this newsletter is a story that shows the impact of CR&T's commitment to research – past, present, and future. The story begins nearly 20 years ago, when Novartis Pharmaceuticals asked Dr. Richard Silver, CR&T's founder, to be one of the principal investigators in a national, multi-center study of imatinib, a promising new treatment for chronic myeloid leukemia (CML). At the time, there were no effective therapies for this deadly blood cancer, and doctors could offer little hope to their CML patients.

Imatinib proved to be a medical breakthrough. Remarkably, of the study participants who were treated with the drug in 1999 and 2000, 80 percent are alive today. One of those patients, Dr. Bharat Shah – who had been told that he would have no more than three years to live – will receive CR&T's Humanitarian Award at our Cancer Survivors Hall of Fame Dinner on November 14 (see page 5).

In 2001, imatinib became the first CML drug to receive FDA approval. Since then, other CML therapies that are closely related to imatinib have been developed. Today, Dr. Silver and other investigators at the Richard T. Silver, MD Myeloproliferative Neoplasm Center continue to explore these and other options for people with CML (page 2).

As our cover story shows, this is one example of many. Thanks, in large part, to CR&T's multi-million-dollar investment, the Silver Center is rapidly becoming a hub for innovative research collaborations. A Weill-Cornell team that includes Dr. Joseph Scandura, the Center's scientific director, and Dr. Shahin Rafii, a member of our Medical Advisory Board, recently discovered a way to make an unlimited supply of healthy blood cells from the cells that line blood-vessels (page 2). This achievement marks the first time that any research group has generated such blood-forming stem cells.

The researchers published their findings in the May 17 issue of *Nature*, one of the world's most-cited scientific journals.

If this method can be applied to humans, its impact will be enormous. "It might allow us to provide healthy stem cells to patients who need bone marrow donors but have no genetic match," says Dr. Scandura. "It could lead to new ways to cure leukemia and myeloproliferative neoplasms, and may help us correct genetic defects that cause blood diseases like sickle-cell anemia."



Dr. Richard Silver with visiting professor Dr. Richard M. Stone (center) and Weill Cornell fellows

CR&T's support of the Richard T. Silver Visiting Professorship at Weill Cornell is yet another way that we encourage valuable exchanges of knowledge and ideas. Each year, a distinguished expert from another institution is invited to give a lecture on a key topic. The 2017 speaker was Dr. Richard M. Stone, Professor of Medicine at Harvard Medical School, whose talk focused on "New Directions in Acute Myeloid Leukemia."

All of us at CR&T – and, most importantly, the patients and families we serve – are deeply grateful for your very generous support. We would be delighted to thank you in person at one of our events this fall: our MPN Patient Symposium, which will take place on November 1, or our Cancer Survivors Hall of Fame Dinner, which will be held on November 14. And, as always, we look forward to sharing more research news in our next issue. In the meantime, we wish you and yours a healthy and enjoyable summer.

Sincerely,

Thomas M. Silver, President

SAVE THE DATE!
2017 HALLOWEEN BASH
HOSTED BY CR&T YOUNG PROFESSIONALS
SATURDAY, OCTOBER 29, 2017
More details in our next issue, stay tuned!

CR&T SPONSORS 14TH ANNUAL PROSTATE CANCER SCREENING DAY



Dr. Douglas Scherr and Rev. Patrick O'Connor (first row, from left) with Screening Day staff



Nursing staff

Over the past 14 years, First Presbyterian Church in Jamaica, Queens, has been serving the surrounding community by providing much-needed access to vital diagnostic tests. On April 8, CR&T marked our sixth year as a co-sponsor of the church's Annual Prostate Screening and Health Fair, which offers free prostate, glucose, HIV and blood pressure screenings, along with health education classes. Rev. Patrick O'Connor, the pastor of the historic church, and Dr. Douglas Scherr, Professor of Urology at Weill Cornell Medical College, are the organizers of the event. They are joined by dedicated volunteers from health centers and medical schools across New York City, who screen some 200 people in a warm and welcoming environment. No health insurance is required.

According to the Prostate Cancer Foundation, prostate cancer is the most common cancer among men, except for skin cancer. In communities like Jamaica, which has a large African American population, access to screenings is especially important: African American men are 73 percent more likely to develop the disease than Caucasian men. "If caught early, prostate cancer is highly treatable," said Dr. Richard Silver, CR&T's vice president and medical director. "We are proud to support this life-saving program, and to support research that improves the care and treatment of men with prostate cancer." CR&T is currently funding two studies that explore more effective diagnostic and treatment options for the disease, one at the Tisch Cancer Institute at Mount Sinai and the other at Weill Cornell.

For more information about First Presbyterian and its community health initiatives, please visit www.firstchurchjamaica.org.



MEET CR&T's LEADERSHIP: MARIA BRISBANE

Maria Brisbane belongs to a group of highly sophisticated and experienced investment advisors who serve on CR&T's board of directors. A managing director at Merrill Lynch, Maria has more than 25 years of experience in portfolio management for high-net-worth clients, including C-suite executives, entertainers, scientists, and entrepreneurs. She joined CR&T's board in 2009 at the invitation of Michael Kempner, who heads our Investment Committee. In addition to serving on the Executive Committee, Maria has been a co-chair of our Cancer Survivors Hall of Fame Dinner.

As the manager of a biotechnology mutual fund, Maria has a particular appreciation for CR&T's commitment to cutting-edge research. "It's wonderful to be a part of an organization that has contributed to the development of so many important new therapies," she says. "I especially enjoy the scientific presentations at our board meetings – they're a wonderful opportunity to learn about new directions in research that have the potential to change people's lives."

Maria holds a B.A. in English literature and a master's degree in urban and environmental planning from the University of Virginia. Before joining Merrill Lynch, she was a press associate for New York City Mayor Edward I. Koch. She also spent several years in commercial real estate development.

In addition to her work for CR&T, Maria is a member of the Havens Relief Fund Society, The Central Park Conservancy Professional Advisory Committee, and a past advisor to The Grass Foundation, a neuroscience not-for-profit organization. She lives in New York City with her family.

We are deeply grateful to Maria for her dedication to CR&T and the patients and families we serve.

CR&T ANNOUNCES 2017 HALL OF FAME HONOREES

On Tuesday, November 14, CR&T will honor two remarkable men who have overcome cancer. The awards will be presented at our annual Cancer Survivors Hall of Fame Dinner, which will be held at the elegant Essex House in New York City. Once again, NBC 4 New York meteorologist Raphael Miranda will serve as master of ceremonies. We are proud to introduce you to our 2017 honorees, and hope that you will join us for this inspiring evening.



Bharat Shah, PhD **Humanitarian Honoree**

“My story is a testimony to the American Dream – which is still alive and well for anyone who dares to dream,” says Bharat. He left India in 1964, arriving in the United States as a student.

After earning a doctorate in Food Science and Technology from Utah State University, Bharat built a career at RJR Nabisco. A real estate opportunity knocked on his door in 1979 and he risked his entire savings to buy a motel in North Carolina. That one hotel eventually led the Shah family to form Noble Investment Group with headquarters in Atlanta, GA. Founded in 1993, Noble has specialized in making value-added, opportunistic and income-producing investments in upscale and select service hotels affiliated with the Marriott, Hyatt, Hilton and Intercontinental brands. Noble has created thousands of jobs in communities throughout the United States.

Bharat faced one of the greatest challenges of his life in 2000. After a routine physical exam, he learned that he had chronic myeloid leukemia (CML). At the time, no effective treatments were available, and his doctor told him that he had six months to three years to live. Immediately, he and his family jumped on the Internet and began researching the disease. Their search led them to Dr. Richard Silver, CR&T’s vice president and medical director, who was conducting a clinical trial of a new CML drug at Weill Cornell Medical College in New York. Approved by the FDA in 2001, this drug – known as imatinib – has revolutionized CML treatment, saving thousands of lives. Today, Bharat, who lives with his wife Milan in Atlanta, is leading a healthy, active life. Every year, he joins Dr. Silver at Weill Cornell, where he speaks to medical students about his cancer journey.

In 2014, the Shah Family endowed the Bharat Shah Leadership Lecture Series at the Cecil B. Day School of Hospitality Administration at Georgia State University. That same year, Bharat published his autobiography, *America My Destiny*.



Mack Dryden **Cancer Survivor Honoree**

Mack Dryden is a speaker, comedian, and author, and was a staff writer on ABC’s “Politically Incorrect” with Bill Maher. He won two Associated Press writing awards as a reporter in his home state, Mississippi, and finally became a professional comedian who has appeared in several movies and hundreds of TV shows, including “The Tonight Show” with both Johnny Carson and Jay Leno.

A hilarious motivational speaker who has survived both testicular and eye cancer, Mack now travels the country, bringing his message of hope and humor to thousands each year. He has performed for a wide range of clients, including Fortune 500 companies, health care associations, hospitals, and cancer centers.

SAVE THE DATE
Tuesday, November 14
The Essex House · NYC

2017 HALL OF FAME DINNER

To learn more and to purchase tables or tickets, please visit
www.crf.org/Hall-of-Fame-Event or contact Barbara Rosenstein
at 212-288-6604 or brosenstein@crf.org.

LIMITED SEATS AVAILABLE – REGISTER TODAY
9TH INTERNATIONAL PATIENT SYMPOSIUM ON
MYELOPROLIFERATIVE NEOPLASMS

Wednesday, November 1, 2017

Griffis Faculty Club, Weill Cornell Medical College
521 East 68th Street
New York, NY 10065

CR&T is proud to sponsor this full-day event for patients, their families and friends. Learn about the latest developments in MPN research and treatment from distinguished basic scientists and clinical research physicians.

Register online at www.crt.org/9th-International-Patient-Symposium or contact Barbara Rosenstein at 212-288-6604 or at brosenstein@crt.org.

Symposium attendees may attend, free of charge, the *10th International Congress on MPNs and Chronic Myeloid Leukemia: Diagnosis, Management and New Clinical Developments*, a professional education program to be held November 2-3 at the InterContinental New York Times Square.



CR&T NEWS

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ABOUT CR&T

Since 1968, CR&T has funded the world's most promising physician-scientists, equipping them with the resources to advance the treatment of various types of blood cancers, including myeloproliferative neoplasms (MPNs), leukemia, non-Hodgkin's lymphoma, Hodgkin's disease and multiple myeloma, as well as other common cancers, such as breast and lung cancer.

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