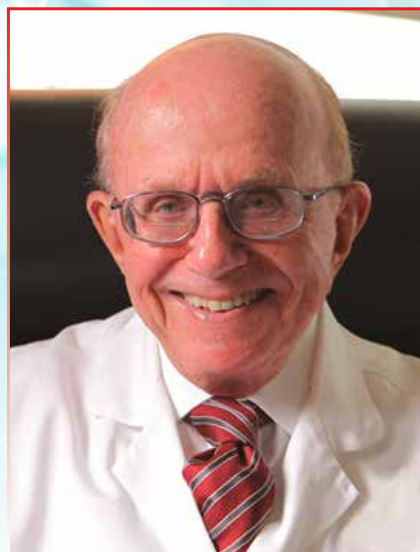


RESEARCH UPDATE: CR&T-FUNDED RESEARCH AT HEMATOLOGY SOCIETY ANNUAL MEETING



From left: Drs. Ghaith Abu-Zeinah, Richard T. Silver, and Joseph M. Scandura of the Silver MPN Center

Despite the impact of the pandemic, 2021 was a highly productive year for CR&T-funded researchers. Six important studies were featured at the Annual Meeting of the American Society of Hematology (ASH) in December. Below are brief summaries of these projects, which were conducted by investigators at the Richard T. Silver, MD Myeloproliferative Neoplasms (MPN) Center at Weill Cornell Medicine, which receives major support from CR&T. The Silver Center research team includes three members of CR&T's Medical Advisory Board: Drs. Ghaith Abu-Zeinah, Joseph M. Scandura, and Richard T. Silver.

Key to many of these studies is the Center's unique polycythemia database (PV), which contains extensive medical information from 470 Weill Cornell patients. The investigators' analysis of this unique scientific resource has generated new insights that could change the face of MPN research and patient care.

Prolonging Patients' Lives

A major study, which first appeared in October 2021 in the high-impact journal *Leukemia*, showed that PV patients treated at the Silver MPN Center have a lifespan that approaches normal in comparison to the U.S. PV population overall. The authors attributed this success to the Center's multidisciplinary treatment approach, which includes early intervention with the drug interferon, as well as close monitoring to prevent dangerous cardiovascular

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complications and progression to myelofibrosis, which causes scarring of the bone marrow and is the most serious type of MPN. The practices outlined in this study could lead to new guidelines for monitoring and treating PV at

centers nationwide and abroad. (For a video overview from Ghaith Abu-Zeinah, MD, one of the authors of the study, please visit www.crt.org/Updates.)

A related study compared the mortality of younger MPN patients – those under 60 – to older patients with these blood cancers. Based on the current diagnostic criteria, young patients tend to be classified as low risk. As a result, physicians may manage their disease through observation or by prescribing only aspirin or phlebotomy, rather than more powerful therapies. But the Silver Center researchers found that the lifetime risk of mortality is *higher* in patients diagnosed at a younger age. Early intervention with therapies such as interferon may prevent severe complications or disease progression in this group, which could also benefit from greater access to clinical trials. The researchers recommend that the current treatment criteria be revised accordingly.

Which PV Patients Are at the Highest Risk for Blood Clots?

PV patients are at high risk for blood clots (thrombosis), which can lead to a heart attack or stroke. Joseph M. Scandura, MD, PhD, the Center's Scientific Director, led this project, which used electronic patient records, machine-based learning, and artificial intelligence to determine which patients are at the highest risk for this complication. After an analysis of more than 100 parameters, the team found that four major factors predict which patients are most likely to experience thrombosis: time since diagnosis, age, time since last blood clot, and body mass index. This new model may allow doctors to monitor and treat patients more effectively, ultimately preventing life-threatening complications. In addition to being featured at an ASH poster session, this study received the Outstanding Abstract award at the 2021 International Congress on MPNs, which was held in October.

Predicting PV Disease Progression

Identifying PV patients who are most likely to progress to myelofibrosis is crucial. Using a machine learning algorithm to analyze data from 527 patient records, this multicenter study identified the clinical features that predict the risk of progression. In addition to helping physicians to monitor high-risk patients, this new model could identify qualified participants for clinical trials of new treatments that have the potential to prevent progression.

Evaluating the Role of an Enlarged Spleen in PV

Although an enlarged spleen (splenomegaly) is considered a hallmark of PV, little is known about how frequently

splenomegaly occurs and how closely it is associated with the signs, symptoms and prognosis of PV. Surprisingly, this systematic study of splenomegaly found that 85 percent of PV patients have a normal or minimally enlarged spleen at diagnosis. Moreover, 12 years after diagnosis, spleen enlargement was not associated with decreased survival. Thus, many patients do not need extensive – and expensive – imaging to measure spleen size. The exception was younger patients who developed significantly enlarged spleens. Importantly, any patient who experiences this complication must be monitored carefully, since it may be a sign of more aggressive disease.

Developing a New Biomarker for MPNs

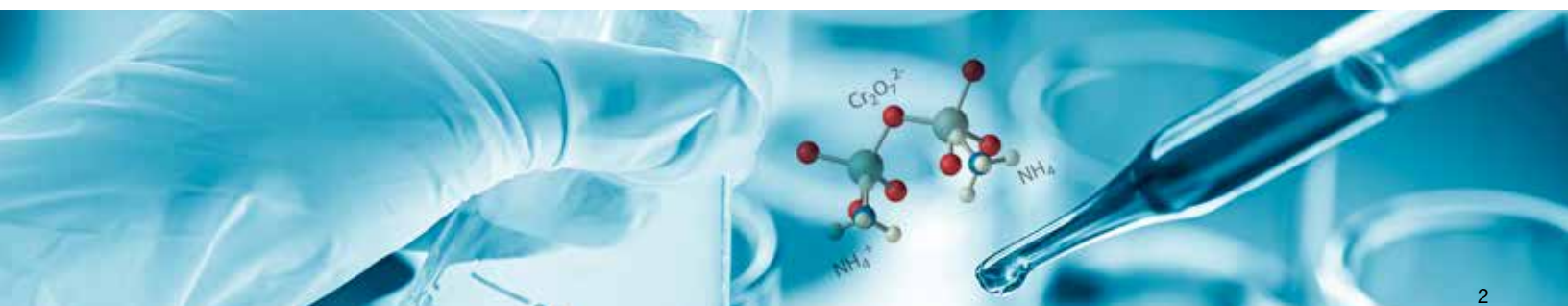
To help evaluate potential MPN therapies during clinical trials, researchers need effective biomarkers. A biomarker is a molecule in the blood or tissue that can serve as a “stand-in” for a process that would normally take a long time to evaluate, such as long-term survival or how well a patient responds to treatment.

Hemopoietic stem cells are immature cells that can develop into all types of blood cells. MPNs originate from hemopoietic stem cells that have a mutation known

as JAK2V1617F. This mutation provides the MPN cells with *fitness* – the ability to outcompete normal stem cells for growth and survival. Based on a study of more than 100 patients with the JAK2 mutation, Silver Center investigators found that MPN fitness can be measured from routinely collected blood samples. As a biomarker MPN fitness can play two roles: as a prognostic biomarker that identifies patients who are at high risk for complications or disease progression, and as a monitoring biomarker that can be used in clinical trials to predict long-term outcomes. The team is now developing methods to simplify routine measurement of MPN fitness for use in clinical trials.

Since 2011, CR&T has invested more than \$7 million to establish the Silver MPN Center and ensure its continued growth. We wish to acknowledge The David L. Johns Family and The Applebaum Foundation for their generous multi-year research grants, as well as the many dedicated friends who make our achievements possible (see page 5). To learn more about CR&T and the Silver MPN Center, please visit www.crt.org/the-silver-mpn-center.

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MESSAGE FROM THE PRESIDENT



All of us here at CR&T wish you and yours a happy and healthy New Year. These are challenging times for individuals and organizations alike, but thanks to friends like you, 2021 was a highly successful year for CR&T. We netted more than \$1 million, far exceeding our projected revenue for the year

– the result of our donors' generosity and the careful stewardship of our investments. Most important, 78 cents of every dollar we spent went to crucial research initiatives.

Our cover story focuses on our investment in the Richard T. Silver Myeloproliferative Neoplasms (MPN) Center at Weill Cornell Medicine. The six abstracts featured at the Annual Meeting of the American Society of Hematology (ASH) show the high quality of the research conducted at the Center – studies that are contributing to more effective diagnostic techniques and treatments for the MPNs. Among other important findings, these studies have helped promote the use of interferon, the only drug that can reverse the progression of MPNs, as a first-line therapy for these blood cancers.

Update on the Interferon Initiative

In 2017, a team led by Joseph M. Scandura, MD, PhD, the Silver Center's Scientific Director, was invited to participate in the Interferon Initiative, a three-year, multi-institutional investigation by prominent scientists across the U.S., Europe, and Australia. The Initiative's goal was to uncover a deeper understanding of the mechanisms by which interferon works, and sometimes doesn't work, for MPN patients.

The program, which was coordinated by the MPN Research Foundation (MPNRF), was funded by the MPNRF, CR&T, the MPN Australian Alliance, and PharmaEssentia. The distinguished MPN experts who guided the initiative included Drs. Andrew I. Schafer and Richard T. Silver, the Silver Center's Director and Emeritus Director, respectively.

In November 2021, the MPNRF released a scientific summary, which described each project, its findings, and the resulting publications. It is hoped that the Initiative will lead to further collaborations among the participants, and that their work will contribute to:

- Validating the use of newer, more disease-specific forms of interferon;
- Developing new therapeutic approaches that combine interferon with other drugs; and
- Identifying immune system proteins that enhance the activity of interferon, leading to the development of new treatments.

CR&T was proud to be a part of this important project. To find more information on the Interferon Initiative or to read the Scientific Report, please visit the research website at www.mpnresearchfoundation.org/mpn-interferon-initiative.

What Lies Ahead?

At this writing, the Omicron variant continues to affect our ability to plan for the year ahead. In 2021, our Board of Directors decided to cancel our two major events out of concern for the health of our attendees, many of whom are immunocompromised. We are very grateful to our loyal donors, who continued to support CR&T even though the Cancer Survivors Hall of Fame Dinner, our signature fundraising event, could not take place.

We also wish to thank Heather Newton of Melton Medical Education, the coordinator of the 2021 International Congress on MPNs, for allowing our patients to attend this hybrid professional education program. Sincere thanks, also, to our industry partners for their support of the Congress Patient Program: our lead sponsor, Incyte Corporation; PharmaEssentia; and Sumitomo Dainippon Oncology.

Looking ahead to 2022, we share the world's hope that the pandemic will end, and that we can return to a more normal way of life. In the meantime, our Board of Directors and Medical Advisory Board continue to monitor the situation and to consider our options for the coming year. We will keep you up to date on our plans for our events through this newsletter, our website, and email communications. But you can be sure that one thing will not change: our commitment to advancing research that will lead to new treatments and cures for cancer.

Sincerely,

A handwritten signature in black ink that reads "Tom".

Thomas M. Silver
President

VIDEO RESOURCES FOR MPN PATIENTS



More online resources than ever before are available for people with MPNs. Whether you're looking for the latest research news, treatment options, or tips for coping from day to day, these authoritative sites offer videos featuring respected experts from top MPN centers. All programs are free of charge.

Patient Power (<http://patientpower.info/myeloproliferative-neoplasms>)

An extensive resource covering all types of cancer, Patient Power has articles and videos on every aspect of living with MPNs, including research and treatment, exercise and nutrition, and intimacy and relationships. Speakers include well-known experts and patient advocates. To learn about the latest features, be sure to subscribe to Patient Power's weekly eNewsletter.

MPN Advocacy & Education International (www.mpnadvocacy.com)

This organization "is dedicated to providing the knowledge, support, and resources patients will need as they adjust to living with an MPN through educational symposia in several cities each year, website access, free webcasts of each program, collateral materials, and direction to people, resources and other organizations that can help." Topics of recent webinars include transplants and summaries of MPN drugs.

Texas MPN Workshop (Visit www.youtube.com and search for Texas MPN Workshop 2021)

Held in August 2021, this professional education program brought together MPN experts from around the world to discuss the many new research and therapy options in development for MPN patients. Note: You'll find a link to the full playlist under the first video, titled "Texas MPN Workshop 2021."

VuMedi (www.viewmedi.com)

Although VuMedi is intended for medical experts, patients can sign up to view many expert presentations on MPNs. The selection of videos from the 2021 International Congress on MPNs includes Dr. Joseph M. Scandura's talk on "MPN Stem Cell Fitness and the Link to Clinical Outcomes," which we discuss in our feature article (see page 2).

Voices of MPN – Live Webinar Events (<https://mpnpatientevent.com>)

A patient education program sponsored by Incyte, Voices of MPN offers live webinars that are designed to help patients, caregivers and loved ones to learn about these blood cancers. Using the live chat feature, an Incyte Oncology Clinical Nurse Educator answers attendees' questions.

We hope these resources are helpful! If you know of other websites or programs of interest to MPN patients, we want to hear from you. Please send your suggestions to info@crt.org.



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CR&T's work would not be possible without the generous support of our donors and grantors. We are deeply grateful for their commitment to our mission. The list below comprises supporters who provided gifts of \$500 or more in 2021. For the complete list, visit www.crt.org/thanks-to-our-donors.

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DR. ALISON MOLITERNO TO BE RICHARD T. SILVER DISTINGUISHED VISITING PROFESSOR



The 2022 Richard T. Silver, MD Distinguished Visiting Professorship will be held at Weill Cornell Medicine (WCM) on April 13. This year's speaker will be Alison R. Moliterno, MD, Associate Professor of Medicine in the Division of Hematology at the Johns Hopkins University School of Medicine.

The lecture was named in honor of our founder. It is given by a distinguished speaker from another institution, with the aim of broadening the audience's horizons and perspective. Attendees include the entire faculty, fellows, and house staff of the WCM Department of Medicine, including the Division of Medical Oncology, as well as physicians from Lower Manhattan, New York-Presbyterian Queens, Rockefeller

University, Memorial Sloan Kettering Cancer Center, The Hospital for Special Surgery, and private practitioners.

Dr. Moliterno received her medical degree from the State University of New York at Buffalo, completed internal medicine residency at Johns Hopkins Bayview Medical Center, and hematology fellowship at Johns Hopkins University School of Medicine. In 1998 she was awarded the prestigious Doris Duke Clinical Scientist Award and joined the Johns Hopkins faculty. Her clinical research involves the study of the chronic myeloproliferative neoplasms (MPNs) and is focused on the genetic and epigenetic lesions associated with the MPNs with the goal of improving diagnosis and treatment for these disorders. Her basic research laboratory focuses on the genetic basis of MPN, and developing murine disease models of MPN. CR&T and WCM are proud to welcome Dr. Moliterno as this year's guest speaker.



Cancer Research & Treatment Fund, Inc.
Established 1968

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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