

newsletter

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Commemorative Edition

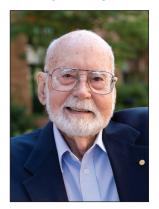
BMT WORLD LOSES TWO OF ITS ELDER STATESMEN

At a time when we are celebrating the major milestone of performing one million transplants, we mourn the loss of two people who made this achievement possible. We dedicate this edition of the CIBMTR newsletter to their memory and to the acknowledgement of their seminal contributions to hematopoietic stem cell transplantation as a life-saving therapy.



In Rememberance of

Dr. E. Donnall Thomas



Written by Fred Appelbaum, MD

Born in Texas in 1920, Don Thomas followed his general practitioner father into the field of medicine. He attended Harvard Medical School where he developed an interest in hematology. In the early 1950s, he became aware of the experiments of Leon Jacobsen and others, showing that marrow of normal mice could be destroyed by radiation and replaced by marrow from a normal donor. With that knowledge, Don became convinced of the clinical potential of marrow transplantation. In 1955, he moved to the Mary Imogene Bassett Hospital in Cooperstown, New York, to join Joseph Ferrebee. There, in 1956, they performed the first human marrow transplants. Although some success was seen in identical twins, transplants between siblings uniformly failed because of graft rejection or graft versus host disease. Don turned to a canine model of transplantation, and over the next decade, first in Cooperstown and then in Seattle starting in 1963, he and his colleagues figured out the basic requirements for transplant compatibility, for a safe and effective preparative regimen, and for the use of post-transplant methotrexate to prevent lethal graft-versus-host disease. With this foundation, in the late 1960s, he returned to the clinical challenge of human transplantation. The early years of clinical transplantation were particularly challenging; the patients were extremely ill, support systems were rudimentary, and the medical community was highly skeptical. However, Don was able to show that allogeneic marrow transplantation could, indeed, cure otherwise incurable patients, and that set the stage for all that has followed.

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In Rememberance of

Dr. Karl Blume
1937-2013



Written by Rob Negrin, MD

Karl Blume was a pillar of the Bone Marrow Transplant Program, Cancer Institute, Stanford and transplant communities. Karl received his medical education at the University of Freiburg, Germany. He came to the United States in 1971 as a postdoctoral fellow working with Dr. Ernie Beutler. After returning to Germany, he was recruited back to the United States to form the bone marrow transplant program at The City of Hope National Medical Center in Duarte, California. He led that Program to international prominence as the Head of the Department of Hematology and Bone Marrow Transplantation, and he left that program in the able hands of Steve Forman who continues as the Director. Karl was recruited to Stanford in 1987 to build a transplant program that he developed into one of the leading programs in the country. During that time, Karl led a Program Project Grant and the Division of Blood and Marrow Transplantation. Karl recruited myself and Nelson Chao to his team. Nelson went on to become the head of the bone marrow transplant program at Duke University, which has thrived under his leadership.



IN REMEMBRANCE OF DR. E. DONNALL THOMAS

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Don was extremely bright but always anxious to learn more. If you were working in an area he was unfamiliar with, he'd stop by and modestly ask for a lesson. He was soft spoken and would let others lead most discussions, but he projected a remarkable aura of authority. When he did speak, everyone would stop and listen. He could be a stern critic. You didn't miss a due date or send him a poorly prepared draft manuscript or grant proposal. At faculty meetings, if someone dared to make a joke, no one would laugh unless Don did. Then everyone would laugh until Don stopped, and then everyone would stop. At heart, though, he was modest and extremely generous, deflecting praise to his co-workers to whom he was very loyal, and we, of course, felt blessed to be able to return that loyalty.

There are many aspects of Don's approach that are extraordinary, but two deserve specific mention. First, he truly believed in the concept of marrow transplantation and was willing to bet the farm on it. While other cancer centers were concerned about becoming "comprehensive", Don focused almost the entire clinical efforts of the Fred Hutchinson Cancer Research Center on marrow transplantation. A second aspect of Don's approach was his appreciation that if marrow transplantation was going to work, it would take a team to do it, including nurses, lab techs, administrators, and medical subspecialists focused on the entire spectrum of complications his patients might develop. When Don learned that he had been awarded the Nobel Prize, one of the first places he went was to the transplant unit's nursing station to thank the nurses (whom he called his secret weapon).

While Don was extremely hard working, he also appreciated that there was life outside of work. When faculty candidates came to visit Seattle, Don would jokingly ask them if they were skiers or fisherman because he wanted to balance the two to ensure that enough people would be at work both winter and summer. He and his wife Dottie were avid hunters and fisherman, and every meal we shared at Don's house came courtesy of their rod or gun. They particularly enjoyed having new faculty over their house, and it never got old watching Don take a new recruit over to a picture of Dottie holding a shotgun in one hand and several dead ducks in the other. He would advise the recruit, with only a slight smile, that it would be best if they got their papers in to Dottie on time.

There are few true heroes in the world. Don was ours.

- Performed the first human bone marrow transplant in 1956 and pioneered the use of hematopoietic stem cell transplantation to treat malignant and non-malignant disorders.
- Served as the first Director of Medical Oncology at the Fred Hutchinson Cancer Research Center starting in 1974 and led its development into a premier center for transplant research and clinical care.
- Awarded the Nobel Prize in Medicine in 1990.

IN REMEMBRANCE OF DR. KARL BLUME

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Therefore, Karl was responsible for at least three of the major BMT programs in the United States, not to mention the legions of fellows that he trained and mentored. Karl was known for his rigor in clinical trials of transplantation and also for implementing team based treatment concepts incorporating all aspects of the care team that is modeled in many other areas of the medical center to this day. In 2000, Karl stepped down from the Division Chief role in the BMT Division at Stanford to be a driving force in the development of the Stanford Cancer Institute.

Karl was known for his dedication, discipline, compassion and sense of humor. He was a particular fan of Stanford athletics and knew at all times the updated scores of the Director's Cup competition. Karl was a forceful and effective mentor and took great pride in his mentee's accomplishments. From personal experience, he was as happy as I was when I received funding for my first R01.

Karl was a critical driving force for the development of ASBMT and the Biology of Blood and Marrow Transplantation. He became the first honorary member of ASBMT and the first co-editor of BBMT. Karl won many awards and honors, both in the United States and Germany, but his legacy is the impact he had on the thousands of patients that he treated. He was unique, and all who knew him were deeply touched.

- Served as Head of Hematology and Bone Marrow Transplantation at The City of Hope National Medical Center starting in 1975.
- Served as the first Director of the Division of Bone Marrow Transplantation at Stanford University starting in 1987.
- Cooperatively founded the American Society for Blood and Marrow Transplantation in 1994, and served as the first Editor-in-Chief for its scientific journal, *Biology of Blood and Marrow Transplantation*.

Remembering Dr. E. Donnall Thomas

Don Thomas's legacy is enormous - he can truly be called the founding father of the field. The value of his contributions to the lives of patients and the countless trainees with whom he had contact throughout his career as well as his contribution to the establishment of the IBMTR and the scientific understanding of the basis of hematopoiesis and transplant immunology cannot be overstated. These accomplishments were fittingly recognized by his receiving the Nobel Prize in Medicine in 1990, the highest award for scientific achievement in a given field.

To have done all this with humility, gentleness, and grace makes this an even greater achievement. While many great teachers like Dr. Thomas have served as mentors to students of all levels, it is rare indeed to identify an individual who can honestly be described as the mentor for an entire field. Although his contributions will live on forever, we remain both saddened by his passing and inspired by the leadership he provided to a discipline that remains at the forefront of both the art and science of medicine.

Thomas Shea, MD University of North Carolina

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For many of us, he was our teacher and scientific father. He formed our approach to scientific problems and helped us in understanding stem cell transplantation. We will keep him in our heart with enormous gratitude and will let Dottie know that we are very close to her.

Dietger Niederwieser, MD WBMT President

As many know, Dr. Thomas spent part of his career as physician-in-

chief at the Mary Imogene Bassett Hospital in Cooperstown, where I was born. Early on in my training in pediatric heme/onc, I became fascinated with transplant. During a visit to my parents' home, I recall dragging along a raft of articles on transplant, including Dr.

Thomas's article from the New England Journal of Medicine. My mother was especially interested in his article—noteworthy because she had no connection whatsoever with medicine, cancer, or transplant—or so I



thought. It turns out that my mother was one of Dr. Thomas's earliest transplant donors. She'd been admitted to the Bassett in the 1950's for elective surgery. As the story goes, Dr. Thomas met her and asked if she would be willing to donate her marrow for a young man with poor risk leukemia. She happily agreed (and had the callous to prove it).

Susan Parsons, MD, MRP Tufts University School of Medicine



I was privileged to be accepted by Don Thomas to do a post doc in Seattle in 1978-1979. It was a gift to have Don Thomas and his team as teachers in allogeneic hematopoietic stem cell transplantation. To participate in rounds when Don was attending was magical. He was like a walking medical textbook and knew absolutely everything in medicine, not just stem cell transplantation. Thanks to Don

and his team, I had the opportunity to build up hematopoietic stem cell transplantation in Sweden after my return to the Karolinska Institutet.

Don came to Stockholm several times to give lectures on recent advances in stem cell transplantation. The first time he came alone, the second time he brought Dottie, and the third time he brought his whole family and then he also got the Nobel Prize in Medicine. There are so many patients and colleagues worldwide that can thank him for so much. I am proud to know him and his team as a friend. I am happy that my country could provide him with a prize that highlighted his achievements in medicine and what he has done for humanity.

Olle Ringdén, MD, PhD Karolinska University Hospital

When I came to Seattle in 1978 to train in bone marrow transplantation, Dr. Thomas encouraged me to continue to develop the field. Then he was my guest in Israel with Dottie, and he helped me start my program out of scratch, with no budget, just with strong will. He even helped me overcome all the skeptic physicians that did not understand the therapeutic potential of allogeneic stem cell transplantation.

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When I traveled to Seattle again, he insisted I stay at his place, not a hotel. I will never forget that the following morning, when I had to catch an early flight, he insisted on taking me to the airport. He wouldn't allow me to call a cab. That's the kind of friend he was.

Shimon Slavin, MD
The International Center for Cell Therapy and Cancer
Immunotherapy in Tel Aviv, Israel

REMEMBERING DR. E. DONNALL THOMAS

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I first met Dr. Thomas in San Francisco in 1990 at the International Congress of the Transplant Society. I was then a young transplant physician, having recently started a transplant program at my institution in Lisbon, Portugal. When I was introduced to Dr. Thomas, he took a special interest in my activities and even invited me to join him for lunch. Such a kindness from such a great man and scientist impressed me very much. I shall never forget this great lesson.

Manuel Abecasis, MD, PhD Instituto Portugues Oncologia

I had the privilege of knowing Donnall Thomas as early as 1987 when, after the Chernobyl disaster, a need for bone marrow transplants rose immensely and I, together with my friend Valery Savchenko, received an opportunity to work for a couple of months in Seattle with Donnall Thomas.

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Although my stay at Seattle was brief, it changed my professional way completely. It was my pilgrimage to Mecca of hematopoietic stem cell transplantation.

While in Seattle, we perceived the mysteries of BM transplants revealed to us by world-famous experts and great scientists: Reiner Storb, Dean Buckner, Wiiliam Bensinger, Alexander Fefer, and Robert Hickman. What was most important, though, was that every day we had the opportunity to communicate with Dr. Donnall Thomas.

I was immensely impressed not only by his undeniable professional qualifications, depth of mind and ability to concentrate, but also by the nobility of his nature, ease of communication and his wisdom. He never avoided communicating with us, sharing his ideas freely.

Boris Afanasyev, MD Saint Petersburg State Pavlov Medical University

One cannot speak of E. Donnell without speaking also of Dotty. She complemented his genius and dedication – and knows the recipe for the best Grav Lox. I learned something each time I visited Seattle. The "blackboard" included organization, the highest standards of patient care, and how they were combined to epitomize outstanding science.

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I feel privileged to have known Dr. Thomas, to have been seen him at work at play, and to have been inspired by his life's work.

Roy S. Weiner, MD
Tulane University Health Sciences Center



At the award ceremony at the Stockholm Concert Hall on the 10th of December 1990, I had been given the honor of presenting Don's contribution to science - the reasons he had received the prize - in five minutes. However, the tough secretary of the Nobel assembly,

Stig Ramel, who organized the festivities, required a rehearsal of the entrance ceremony. The laureates had to appear in the morning for rehearsal together with the presenters. Don was supposed to walk with me at his side. Although he certainly accepted this arrangement, I realized that he was looking for Dottie. He seemed a little confused since she was not even allowed to participate in the rehearsal. However, at the real ceremony, Dottie was in one of the front rows. Don was happy, and all went well. My presentation seemed to be appreciated by this giant in clinical science.

Gösta Gahrton, MD, PhD Karolinska University Hospital



Though I had seen Don from afar and was well aware of his pioneering work from my earliest days in BMT, my first personal meeting with Don and Dottie Thomas was in 1991 at a

meeting in Santander. I was more than a little intimidated to be speaking on the same program as Don - not only because of his stature in the field and reputation for incisive critique - but also because of the fact that, at the time, there was a certain degree of friction between Seattle and IBMTR (now just history). However, the kindness both he and Dottie extended to me at that first meeting both overwhelmed me and put me at ease - if both things can be true simultaneously. I was also in my first trimester of pregnancy with our third child and struggling with morning sickness and fatigue - Dottie had pity for my circumstances and took me under her wing; her concern and solicitude were touching and something for which I will always be grateful. One of the things I am proudest of is that Don called me to ask to use an IBMTR slide for a Nobel prize presentation. I was thrilled!!! - and sent it right away, of course.

Don's scientific contributions are enormous and will ensure he is remembered by the medical community for many generations - but I think what impresses me most is how much love and loyalty he inspired in the people who worked the most closely with him - that is, in my opinion, the mark of a truly great man.

Mary M. Horowitz, MD, MS Medical College of Wisconsin

REMEMBERING DR. E. DONNALL THOMAS

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When I was a young assistant professor in the early 1990's, one of my first ASH posters was a study documenting the effect of anti-neutrophil antibodies on the rate of engraftment following bone marrow transplantation. As I stood nervously in front of the poster not knowing what to expect, an older man with a white beard approached me and said "Hi, I'm Don Thomas. This is a really interesting study. Keep up the good work." Twenty-two years later, I still tell the story often and consider the exchange as one of the highlights of my academic career.

Thomas R. Klumpp, MD Temple University Bone Marrow Transplant Program

I had the privilege of working with Dr. Thomas and his team as a visiting fellow in Seattle in 1993-1994. The "Seattle School" has left a definite imprint on the scientific, medical and personal life of hundreds of transplanters all over the world. This is



because of the example Dr. Thomas set, including his inspiring way of doing things at the bedside (with compassion and real interest for the patients) and at the laboratory (with talent and very hard work), but also as a human being (because of his humility, his generosity and fine sense of humor). Dr. Thomas came to Murcia, Spain, to help us start our BMT Program. We will never forget his lessons ("The team, mainly the nurses, and the mind focused on the patient, are the most important principles in a BMT Unit") and his enthusiasm to teach the youngsters. The Spanish BMT community owes an immense debt of gratitude to this great man. Here in Murcia we will always have his memories as an example to follow.

Jose M. Moraleda, MD, PhD University of Murcia

All of us who have had the chance of helping someone with a bone marrow transplantation, throughout the world, will always keep this generous and bright man within our hearts, our souls. Dr. Thomas, thank you so much for everything you brought to humanity.

Vicente Odone-Filho, MD, PhD São Paulo University Medical School



On October 4, 1994, Dr. Thomas and his wife visited the Bone Marrow Transplantation Unit of Ankara University Hematology Department. As Turkey's young, dynamic and pioneering transplant physicians, the opportunity to be with the father of the transplant (that is, introducing what we had done, visiting our patients, and having a happy meal) was a very charming moment to be remembered. This old photograph of those moments reflects excitement, ambition, anticipation, pride and gratitude. The spark of science in those young physicians increased with the appreciation and encouragement of Dr. Thomas.

Gunhan Gurman, MD Ankara University Medical School

Very early in my career, while attending an ISCT meeting at the Hyatt in downtown Vancouver in the late 1990s, I got out of bed very early and decided to go up to the top floor meeting area to see if breakfast was being served. When I entered the area set aside for breakfast, I noticed that there were only two other people in the room - an older gentleman and his wife quietly holding hands and looking out over the Vancouver skyline. He must have heard me come out of the elevator because he turned around and greeted me, asking where I had come from to attend the meeting. When he spoke, I noticed that he was wearing a gold lapel pin, and on closer inspection, I realized that it was a replica of the Nobel medal. It was then that I knew to whom I was speaking. I have since seen him several times at various places around the country where hematology and BMT meetings are held, but I will always remember him as the older gentleman holding hands with his wife and sharing the beauty of the early morning view of Vancouver.

Lawrence S. Lamb Jr., PhD University of Alabama at Birmingham

Remembering Dr. Karl Blume

We remember him as a unique mentor, an excellent teacher, a dedicated physician and a real gentleman. His ideas and comments were always welcome and wise. In the most difficult situation, he had the right answers, and he has to be acknowledged for the success of stem cell transplantation



worldwide. We miss a dedicated scientist, a compassionate physician and a unique friend in the stem cell transplantation world.

Dietger Niederwieser, MD WBMT President

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I first met Karl while I was at UCSD and he and Steve Forman took me under their wings. As the new kid on the west coast block, he made sure I was included in everything from discussions with State agencies to revelry at the early Keystone meetings. Not only was he an inspirational thinker and teacher, but he added a wonderful sense of humor, camaraderie, and grandeur to our field. I still have very fond memories of the time I was at Stanford in 1992. We had a special evening at his house, reflecting on medicine and life in general while enjoying a dinner and his backyard gazebo. He was someone who would often go out of his way to stop by a poster or presentation at national meetings – to say hello and both congratulate and critique your effort, usually at the same time!

Our field has lost a true gentleman, scholar, and statesman whom I, and many others, will also miss as a friend and mentor.

Thomas Shea, MD University of North Carolina

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Karl was integral to the growth of the BMT field, directly saved the lives of thousands of patients, and mentored hundreds of young investigators who continue to advance our field around the world. He was a solid example of integrity as supported by both words and actions. He frequently stated, "You must do what is right, no matter how difficult." Karl had very high standards, but he was always supportive and always fair. He was a priceless mentor, a gracious colleague, a trusted confidante and a thoughtful friend. I could ask advice anytime about work, career, patients, life in general, or for a thoughtful critique on a current project. He was my "rock". Karl also embraced life...he loved sports and appreciated the arts, fancy cigars, and a good laugh. There will never be another Karl.

Ginna G. Laport, MD Stanford University Karl has been a major leader in hematopoietic transplantation for half a century. He founded the City of Hope and Stanford Programs, which have been innovative leaders in research and patient care. He was an international leader that was a key participant in the formation of NMDP and ASBMT. We were all inspired by him as a role model and will miss him.

Richard E. Champlin, MD MD Anderson Cancer Center

One of my brightest memories of Karl was the encouragement he gave me (in a 15 second elevator ride) after my first ASH presentation almost 25 years ago. Nothing over the top - but direct, warm and completely authentic, like the man himself. Our world is a little smaller without Karl.

James Ferrara, MD University of Michigan

Dr. Blume was beloved, deeply valued and truly unforgettable. Committed to excellence, unwavering in his support for patients, rigorous in his value for research and education, he built one of the world's most successful stem cell transplant programs, laid the critical foundation for the Stanford Cancer Institute, mentored and guided countless students, trainees and faculty, and deeply loved his family and Stanford. I value my friendship with Dr. Blume exceedingly and will miss him tremendously. He leaves an indelible mark on all of us.

Philip Pizzo, MD Stanford University



Like so many others, I remember Karl as an unusual combination of sternness and kindness, with extremely high expectations but generous in his mentorship and assistance, having total focus on the task at hand but great capacity for humor and joie de vivre. He was the kind of person you just never

wanted to let down. About a dozen years ago, we discovered that we shared an interest in European soccer - it was great fun following the World Cups with him by email. He was so passionate about the sport, I almost had to root for Germany (and generally did once the US was eliminated)! Wish they could have given him a title to enjoy.

Mary M. Horowitz, MD, MS Medical College of Wisconsin

REMEMBERING DR. KARL BLUME

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Karl was an extraordinary man, and he will be greatly missed by many. He was truly a gentleman, a scholar, and - by every measure - a wonderful human being. My hope is that all who were influenced by Karl will strive to model our lives after the wisdom, caring, dedication, integrity, and enthusiasm, which he taught by example. It will make the world a better place.

Michael Amylon, MD Stanford University

I first got to know Karl as a first year fellow in 1998. What stands out for me is that he made you feel important -- as a trainee, this confidence is key: that both individually, and as part of a team, you could achieve great things if you were focused and worked hard -- he modeled this; and you knew he had your back to make it happen.

Jason Robert Gotlib, MD Stanford University

Karl was a giant in the field and a true gentleman liked by all. There are few who have been such pioneers in the field and whose life's work focused so deeply on improving the lives of patients undergoing

HSCT. His contributions were remarkable, and his legacy will continue robustly with his many trainees and colleagues who benefited from his tireless energy and enthusiasm.

Bruce Blazar, MD University of Minnesota

Karl was a kind person and always interested in what we lab folk had to say. I remember being introduced to him by Bonnie Cunningham at one of the first ASH meetings I attended, when I knew people from their reputations only. He was somewhat formidable, looking down from his height with very astute questions, but whatever hesitation I felt was dispelled by his joking and the fact that he included me in the banter - then even remembered my name. The world of transplant has lost another of the great ones.

Nancy H. Collins, PhD Memorial Sloan-Kettering Cancer Center

We have all made what little progress that we each have made by, in part, walking on the shoulders of giants. There have been few giants in our field that have moved the field of stem cell transplantation further ahead than Karl. Not only was he a visionary but always someone who seemed to have a healthy respect for the rigors of well-designed and executed clinical trials, someone who was always excited by the science of transplantation immunology. Finally and most importantly, he was always exemplary in his commitment to teaching, patient care and mentoring so many of us in the field that his life has touched.

John F. DiPersio, MD, PhD Washington University School of Medicine Karl was clearly one of the giants of the field. Others have commented on his great intellect, but I would have to say that he was one of the special ones who possessed wisdom, in addition to great intelligence. And yet, it is his personal warmth and character that I will miss most. Nothing was ever superficial with Karl. Everything was deeply felt and genuine. My closest working association was as ASBMT secretary when, in the early years, his personal commitment helped transform BBMT from a struggling journal to the pride of the society. It was largely his sheer force of will that helped make that happen. He was a wonderful role model in every way.

Neal Flomenberg, MD Thomas Jefferson University

I admired Karl's remarkable combination of rigor, compassion, and humor. He kept us on the right track in the development of the Cancer Institute, leading by example, always firm but fair, always with the best in mind and the will to see that we made it happen. I talked with him just a few weeks ago at a Cancer Institute leadership meeting, with his oxygen. He was in such good spirits and undaunted by the obvious limitations it indicated.

I will never forget seeing him in the parking lot outside the Medical School one evening many years ago. He was walking uncharacteristically slowly, head bowed. I asked him how he was. He replied, "I was just with a patient on the Unit who was sicker than any human should ever be." I was and am touched by the depth of his caring for his patients and their suffering.

We will miss him deeply at the Cancer Institute and the School of Medicine. He made me proud to be a physician and colleague. We are so much the better for having known him all these years.

David Spiegel, MD Stanford University

We all wish he could have gone on forever with his remarkable joy of life and ability to inspire others to excel. While he leaves behind a lifetime of accomplishments, which will be much reiterated, he was perhaps most impressive in his unique ability to make everyone from patients to staff and colleagues feel special and deserving.

It is always hard to know how to honor a person who has profoundly helped and touched so many lives. But even in this time of sorrow, he definitely would want us all to greet each day humming, "Oh what a beautiful morning, oh what a beautiful day..."

Maureen Ross MD, PhD Roswell Park Cancer Institute

CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

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