ASBMT eNews

AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION

November 2012

A WORD FROM PRESIDENT ELIZABETH SHPALL, MD

E. Donnall Thomas was a Giant in Medicine

As we review grants, consider the merit of new faculty, create meeting programs or simply think about how we can improve the care of our patients, we are always alert for concepts that change the paradigm of what we do. No one in our field embodied this concept more powerfully than Don Thomas.

Dr. Thomas' scientific and medical accomplishments were recognized in 1990 with the Nobel Prize, a richly deserved award. Many of us who were inspired by him recognize Dr. Thomas for several very specific achievements as well. Perhaps, most importantly, his persistence in the face of doubt from many of his contemporaries is inspiring.

In collaboration with his colleagues and his many brave patients, our field was born. Between the 1957 publication of his original allotransplant experience for advanced leukemia and the 1979 article describing the use of allotransplantation for leukemia in first remission, a number of scientific and practical barriers had to be overcome. The use of total body irradiation to condition the recipient, the use of tissue matching in a broad clinical context, the importance of induction therapy to reduce disease burden, and overcoming difficult treatment and infectious toxicities were all critical to his success. Placing these fundamental ideas in an overarching, conceptual context made his contributions extraordinary.

Perhaps most striking, however, was the practical recognition that leukemia was a uniformly fatal problem that needed to be overcome and that he had a team of willing patients, committed collaborators and a scientific framework that justified effort in the face of doubt and criticism over the high-risk nature of his treatment program. When we look today at what he accomplished over those 22 years, we can only marvel at his persistence, courage and insight.

In addition to his own accomplishments, he was an inspiration to a generation of physicians and scientists who sought to learn from his example and expand in some small way on his

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ideas and treatment concepts. In addition to his colleagues in Seattle, many of us around the world were inspired by knowing him, observing his kind and supportive interactions, yet noting his devotion to scientific rigor and pursuit of ever better outcomes for our patients.

As we reflect on his life, how could we find a more compelling example of a man who left the world a better place than he found it through the power of his ideas, commitment and example? I am sure that he would want all of us to honor his memory by rededicating ourselves to press ahead down the path on which he pointed the way.

-Elizabeth Shpall

Clinical Research

Unrelated Marrow and PBSC Transplant Outcomes Compared

A phase 3, multicenter, randomized trial conducted by the Blood and Marrow Transplant Clinical Trials Network compared outcomes of 551 patients who received either a peripheral blood stem cell (PBSC) or bone marrow transplant from an unrelated donor. The patients who received a PBSC transplant had a survival rate of 51% two years after transplantation compared with 46% in patients who received a bone marrow transplant (p=.29), according to the results published in the *New England Journal of Medicine*. In addition, the overall incidence of graft failure was lower for PBSC transplant patients (3%) compared to bone marrow transplant patients (9%). However, the likelihood of chronic graft-versus-host disease (GVHD) was higher in the PBSC group (53%) than the bone marrow group (41%), but there were no significant differences in acute GVHD or relapse between the two groups. The authors concluded that there was no significant survival difference between the two groups. More...

How Genetic Disparity with MHC and non-MHC Affects Allogeneic HCT Outcome

This article published in *Blood* reviewed the influence genetic identity or nonidentity between donor and recipient at loci both inside and outside the MHC can have on allogeneic hematopoietic cell transplantation (HCT). Although differences within the MHC are the most important risk factors for the development of severe graft-versus-host disease (GVHD), disparity at loci outside the MHC that encode minor histocompatibility (H) antigens can elicit GVHD and graft-versus-leukemia activity in donor/recipient pairs who are otherwise MHC identical. Minor H antigens are generated by sequence and structural variations within the genome. The total number of minor H loci is probably large and ensures that all identical MHC donor/recipient pairs will mismatched for many minor H antigens. In addition to minor H loci, unrelated donor/recipient pairs exhibit mismatches at numerous loci within the MHC, particularly HLA-DP, Disparity at HLA-DP exists in 80% of unrelated pairs and significantly influences the outcome of unrelated HCT. More...

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BMT Tandem Meetings

Registration for BMT Tandem Meetings
Please remember that registration for the 2013 BMT Tandem Meetings to be held Feb. 13-17 in Salt Lake City, Utah, is open. On a single web page, navigate to meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences. More...

Housing for BMT Tandem Meetings
Hotel reservations are first come, first served. Please remember that February is a popular vacation month in Salt Lake City. On a single web page, navigate to meeting registration, housing reservations, the preliminary program, abstract submission and parallel conferences. More...

Travel Grants Available for Hem/Onc Fellow
ASBMT members can nominate hematology and oncology fellows for travel grants to attend the 2013 BMT Tandem Meeting in Salt Lake City. Ten grants of $1,000 each will be awarded to introduce young clinicians and investigators to the field of hematopoietic cell transplantation. More...

Clinical Research (continued from page 2)

HLA-Matched Donors Optimal for Nonmalignant Disease Transplants
Researchers analyzed data from 663 unrelated marrow and peripheral blood stem cell transplants performed over a 12-year period to treat nonmalignant diseases to determine the significance of human leukocyte antigen (HLA) matching. According to the results appearing in *Blood*, the researchers discovered that donor transplantations mismatched at the HLA-A, -B,-C or -DRB1, but not –DQB1 or –DPB1, loci were linked to higher mortality and graft failure rates, but were not associated with acute or chronic graft-versus-host disease (GVHD). These results led researchers to conclude that, if possible, patients with nonmalignant diseases should receive transplants from 8/8 allele matched donors. However, if this is not an option, a single allele or antigen-mismatched donor may be used without significantly increasing the risk of GVHD, but increasing the risk of graft failure. More...

Association News

March 1 Deadline for Clinical Research Training Course
The ASBMT Clinical Research Training Course for fellows-in-training and junior faculty is returning to Santa Fe, New Mexico. Applications are being accepted through March 1 for the course that will be held July 10-15. More...

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Basic Science Studies

Heparan Sulfate Advances Acute GVHD After Allogeneic HSCT

Heparan sulfate (HS) can activate Toll-like receptor 4 on dendritic cells in vitro, enhancing dendritic cell maturation and alloreactive T-cell responses. Researchers confirmed in vivo that serum HS levels were elevated at the onset of clinical graft-versus-host disease (GVHD) in mice after allogeneic hematopoietic stem cell transplantation (HSCT), and treatment with the serine protease inhibitor α1-antitrypsin lowered the HS serum levels. This led to reduced alloreactive T-cell responses and GVHD severity. An HS mimetic that increased serum HS levels accelerated GVHD. The study appearing in *Blood* also reports that higher serum HS levels were found in patients undergoing allogeneic HSCT for hematologic malignancies and correlated with GVHD severity. The researchers concluded that HS promotes acute GVHD following allogeneic HSCT and that restricting HS release may have therapeutic potential for controlling clinical GVHD. More...

Signaling Disrupted by Kinase Inhibitor Targets AML

In a study published in *Blood*, researchers used the mTOR kinase inhibitor, PP242, to disrupt interactions between acute myeloid leukemia (AML) cells and stroma. Examining the results in vivo in a mouse model, they discovered several survival signaling pathways that were up-regulated in primary AML cells co-cultured with stroma. PP42 induced apoptosis in samples cultured both with and without stroma and narrowed mTORC1 and mTORC2 activities, sequentially inhibited phosphorylated AKT, S6K and 4EBP1, and concurrently suppressed chemokine receptor CXCR4 expression in primary leukemic cells and in stromal cells cultured alone or cocultured with or without leukemic cells. PP242 was also effective in the in vivo mouse model, inhibiting mTOR signaling in leukemic cells and showing a greater leukemic effect than rapamycin. The findings led researchers to conclude that disrupting mTOR/AKT signaling with a selective mTOR kinase inhibitor can target AML cells in the bone marrow microenvironment. More...

Transplantable Hematopoietic Stem Cells Generated In Vitro

To find a way to selectively generate transplantable hematopoietic stem cells (HSCs) in vitro, researchers of a study from *The Journal of Clinical Investigation* compared different culture systems of bone marrow and embryonic stem cells but found that bone marrow from mice cultured for two months with recombinant IL-7/HGFβ produced the most mature subset of HSCs. They discovered that the adult bone marrow-derived HSCs migrated to the bone marrow and, after intravenous injection, established long-term hematopoietic chimerism. The chimerism level could also be enhanced by an intrafemoral injection of rIL-7/HGFβ. The data from the study show that rIL-7/HGFβ, but not its component cytokines, can induce the generation of at least three subsets of HSCs in vitro, each of which can establish long-term multilineage hematopoietic chimerism in vivo. More...

ASSOCIATION NEWS (CONTINUED FROM PAGE 3)

New! Read BBMT on Your Smartphone

Click here to download Elsevier's HealthAdvance mobile app for your iPhone or Android then log in with your bbmt.org password to gain access to full articles. If you have not yet registered with a username/password on bbmt.org, click here to register and activate your subscription. Enter your ASBMT member or subscriber number when activating for the first time. This password will give you full access to the BBMT website and mobile apps on repeat visits.

BMT Transplant Research Fund

Recently, you received a mailing about *The ASBMT Transplant Research Fund* and the passing of our dear friend and colleague, Thea M. Friedman, Ph.D. Our transplant community, and especially the Amy Program family, has suffered a tragic loss, and we are deeply saddened by this news. We ask that you join us in honoring Thea's life and legacy. As you know, ASBMT is partnering with Be The Match Foundation and the National Marrow Donor Program to increase the number of investigators who are able to pursue their promising research through the Amy Strelzer Manasevit Research Program for the Study of Post-Transplant Complications. With your help and the help of our membership, the first Amy Scholar awarded through our recently established *ASBMT Transplant Research Fund* will be named in Thea's honor. Together, we can offer this tribute to her memory. More...

ASM Research Program

Be The Match Foundation® and the National Marrow Donor Program® (NMDP) are pleased to announce that the Amy Strelzer Manasevit (ASM) Research Program for the Study of Post-Transplant Complications is now open for applications. The ASM Research Program is directed toward scientists and clinicians early in their careers and is intended to advance the understanding of events occurring after allogeneic hematopoietic cell transplantation. One award will be made for a maximum of $240,000 over a three-year period. Proposals must be submitted by Friday, November 2. More...

Interest in New FACT Accreditation Goal Continues to Grow

FACT began accepting applications for its new accreditation goal for cellular therapy processing with more than minimal manipulation. Several facilities have already applied for this accreditation and interest continues to grow. Feedback from applicant facilities has reinforced the purpose of these inspections, which is to help facilities establish processes that comply with FACT's minimum requirements in an effort to promote the quality of their research. While scientific merit is judged by the principal investigators, regulators and institutional review boards, FACT's role is to assist facilities with complying with regulatory requirements and serving their clinical trial sponsors well.

Calendar of Events

•November

GVHD National Symposium
November 2
Independence, Ohio

National Institutes of Health
2nd International Workshop: Biology, Prevention, and Treatment of Relapse After Hematopoietic Stem Cell Transplantation
November 5-6
Bethesda, Maryland

2012 National Marrow Donor Program Council Meeting
November 8-10
Minneapolis, Minnesota

International Conference on Regenerative & Functional Medicine
November 12-14
San Antonio, Texas

Neoplastic Hemapathology Update
November 15-17
Palm Beach, Florida

European Association of Tissue Banks
21st Annual Congress of the Association of Tissue Banks
November 21-23
Vienna, Austria

•December

American Society of Hematology
54th Annual Meeting
December 8-11
Atlanta, Georgia

•January

Cell & Gene Therapy Forum
January 28-30
Washington, D.C.

•February

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 13-17
Salt Lake City, Utah

•March

Association of Community Cancer Centers
39th Annual National Meeting
March 6-8
Washington, D.C.

Canadian Society of Transplantation
Annual Scientific Conference
March 14-16
Lake Louise, Canada

National Comprehensive Cancer Network
18th Annual Conference
March 14-17
Hollywood, Florida

Regenerative Medicine: Technologies Enabling Novel Therapies
17th Annual Hilton Head Workshop
March 20-23
Hilton Head Island, South Carolina

•April

American Association of Tissue Banks
Spring Meeting
April 6-9
Tucson, Arizona

•April (cont.)

American Association for Cancer Research
Annual Meeting
April 6-10
Washington, DC

European Group for Blood and Marrow Transplantation
39th Annual Meeting
April 7-10
London, United Kingdom

Blood and Marrow Transplant Information Network
Celebrating a Second Chance at Life Survivorship Symposium
April 20-21
Costa Mesa, California

International Society for Cellular Therapy
19th Annual Meeting
April 22-25
Auckland, New Zealand

Oncology Nursing Society
38th Annual Congress
April 25-28
Washington, DC

• 2014

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 26-March 2
Dallas, Texas

• 2015

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 11-15
San Diego, California

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Do you have news, responses or opinions to share with us?
Please e-mail the association office at enews@asbmt.org.