

THE COLEMAN FOUNDATION CHAIR FOR BLOOD AND BONE MARROW TRANSPLANTATION



Activities Supported

This report provides an overview of the main patient care and research activities of the Coleman Foundation Blood and Marrow Transplant Center and illustrates how funds from the Coleman Foundation Professor of Blood and Bone Marrow Transplantation supported the transplant program during the time period from July 1, 2009 to June 30, 2010.

Clinical Activities

During this period, approximately 100 transplants were performed. While this number is similar to the prior year, the indications for transplant at Rush have changed. As other competitive clinical trials opened at Rush, the number of lymphoma patients and myeloma patients who underwent autologous bone marrow transplantation (BMT) slightly decreased. Under the leadership of the United States Congress, there is increasing availability of matched unrelated adult donors and cord blood transplants for hematologic cancers. The National Marrow Donor Registry estimated that this type of transplant will increase by 300% over the coming seven years. Thus, the number of allogeneic stem cell transplants performed at Rush also increased.

Activity Report Date

July 1, 2009 – June 30, 2010

Endowment Summary

The Coleman Foundation Professor of Blood and Bone Marrow Transplantation was established in order to advance the bone marrow transplant research program by paying for portions of professional and technical salaries, purchasing supplies and small equipment, and other related purposes.

Chair holder

Henry C. Fung, MD
Director, The Coleman Foundation Blood and Bone Marrow Transplant Center
Director, Section of Stem Cell Transplantation
Professor, Department of Internal Medicine
Rush Medical College

The Coleman Center is in the process of adapting to this new development in the field specifically by establishing new protocols for allogeneic stem cell transplant. Rush recently recruited Dr. Sivadasan Kanangat from St. Jude Children's Research Hospital to serve as the director of the human leukocyte antigen (HLA) laboratory. In collaboration with Dr. Kanangat new donor selection guidelines will be established to identify the best available donor to further improve the transplant outcomes. Dr. Kanangat has brought in new typing technology such as natural killer cell typing and anti-HLA antibody testing.

In August, the Foundation for the Accreditation of Cellular Therapy (FACT) awarded a three-year full re-accreditation to The Coleman Foundation Blood and Marrow Transplant Program for adult autologous and allogeneic transplantation at Rush. The blood stem cell collection program and cellular therapy product processing program, performed by the Rush blood center were also

Activities Supported Continued

re-accredited. The Coleman Foundation Blood and Marrow Transplant Program is a combined effort of the Section of Bone Marrow Transplant and Cell Therapy and Rush Blood Center and has been continuously accredited by FACT since 2001. Currently, 183 programs in Australia, Canada, USA and New Zealand are accredited by FACT and Rush is one of 44 medical centers that has received more than 10 years of accreditation. The program's continuous re-accreditation is a testament to the great effort, commitment and dedicated teamwork of staff and administration to make this a well-established, world-class transplant program.

In October the Coleman Center was selected as a member institution for the Radiation Injury Treatment Network (RITN). The RITN was developed through the cooperative efforts of the National Marrow Donor Program® (NMDP) and the American Society for Blood and Marrow Transplantation (ASBMT). The NMDP and ASBMT collaborated with:

- Department of Defense, Office of Naval Research (ONR)
- Health Resources and Services Administration (HRSA)
- Center for International Blood and Marrow Transplant Research® (CIBMTR)
- Comprehensive Cancer Centers designated by the National Cancer Institute (NCI)
- National Library of Medicine-Radiation Event Medical Management (NLM-REMM)



Rush Endowment Policy

The endowed chair funds of Rush University are subject to Rush University Medical Center's total return policy on endowment, with a portion of the income available for expenditure. The total return policy, set by the Executive Committee of the Board of Trustees, is reviewed annually. The spending policy for the 2010 academic/fiscal year is 3.5% based off a moving three-year average of endowment market values.

- U.S. Department of Energy National Nuclear Security Administration (NNSA) Radiation Emergency Assistance Center/Training Site (REAC/TS)
- Office of Preparedness and Emergency Operations, Office of Assistant Secretary for Preparedness and Response (ASPR), U.S. Department of Health and Human Services
- AABB (formerly the American Association of Blood Banks) International Task Force on Domestic Disasters and Acts of Terrorism
- World Health Organization (WHO) - Radiation Emergency Medical Preparedness and Assistance Network (REMPAN)
- The European Group for Blood & Marrow Transplantation (EBMT) Nuclear Accident Sub-Committee Physicians at the forefront of bone marrow and cord blood transplantation

The RITN was developed to respond to a potential disaster resulting in mass casualties with marrow toxic injuries from ionizing radiation exposure or other hazardous material (such as those caused by sulfur mustard). It is comprised of transplant centers, donor centers and cord blood banks spread throughout the United States and includes most of the prestigious transplant centers. The Coleman Foundation Blood and Marrow Transplant Center is the only member of RITN in the State of Illinois.

Activities Supported Continued

The RITN:

- Develops treatment guidelines
- Educates health care professionals
- Assists participating centers in developing response plans
- Trains participating centers
- Strives to improve center readiness

After a marrow toxic incident resulting in mass casualties, RITN centers such as Rush may be asked to:

- Accept patient transfers to their institutions
- Provide treatment expertise to practitioners caring for victims at other centers
- Travel to other centers to provide medical expertise
- Provide data on patients treated at their centers

Research Activities

Dr. Fung and his associates have participated in multiple clinical trials (detailed on pages 4 and 5). He has also established new collaborations with Dr. Kent Christopherson in the laboratory and Drs. Stevan Hobfoll and Kurrie Well from the Department of Behavioral Sciences.

In collaboration with his colleagues in Behavioral Sciences, he plans to examine the impact of stress, coping, and social support on immune functioning and health status in individuals undergoing stem cell transplant due to cancer. Participants will be assessed regarding their psychosocial functioning at set time -points through the transplant process and their medical records will be reviewed in order to examine graft success, immune recovery and health status. If a relationship exists between immune functioning or health status, and distress, coping and social support researchers will be able to identify patients who are at increased risk for complications or death. This, in turn, will allow them to tailor psychosocial interventions to these patients' needs to decrease their risk for poor outcome after transplant.

In collaboration with Dr. Christopherson, Dr. Fung is co-directing a translational research project to study the best mobilization regimen to harvest blood stem cells, mesenchymal stem cells and endothelial stem cells, which not only have the potential to improve transplant outcomes for patients with cancer, but may also serve as a platform for future studies in regenerative medicine with the potential of enhancing repairs of damaged tissues.

Publications and Clinical Trials

During the 2009-10 year, Dr. Fung authored and co-authored multiple abstracts and manuscripts including publication in premier journals such as **Bone Marrow Transplant**:

Tuncer HH, Gregory SA, **Fung HC**: High-dose chemotherapy with autologous stem cell rescue for relapse after allo-SCT in multiple myeloma: a case report (BMT Oct., 2010)

R. Potru, J Ahn, **H Fung**, S. Cohen A Case of Myelodysplastic syndrome in a liver transplant patient. Transplantation Proceedings, Volume 41, Issue 9, Pages 3947-3948 (2009 Nov)

Henry C Fung MBChB, FRCPE, Sunita Nathan MD, John J Maciejewski MD, PhD. Induction Chemotherapy before Autologous Stem Cell Transplantation for patients with Symptomatic Plasma Cell Myeloma - - - - does it matter? Clinical Pharmacology: Advances and Applications (2010)

The following abstracts were published in **Blood** 2010:

Favorable Outcomes of Neutropenic Enterocolitis Following Hematopoietic Stem Cell Transplantation (HSCT) Using a Conservative Medical Therapy Approach, AM Jimenez, G Behrens, J Maciejewski, N Wool, ES Rich, R Karmali, P Venugopal, SA Gregory, **HC Fung**, and S Nathan;

Cytokine Treatment of CD34⁺ Cord Blood Cells with G-CSF, GM-CSF, or SCF During 48 Hours of *Ex Vivo* Culture Alters CD26/DPPIV Peptidase Activity and Subsequent Engraftment Into NSG Immunodeficient Mice, LA Paganessi, L Luy Tan, S Jagan, R Frank, A Jimenez, ES Rich, S Nathan, J Maciejewski, **HC Fung**, and KW Christopherson

CD26 Inhibition Preferentially Enhances *In Vitro* Migration of G-CSF + Plerixafor (AMD3100) Mobilized PB as Compared to G-CSF Mobilized PB In Multiple Myeloma Autografts, E Yoo, S Jagan, S Palaparthi, MA Enriquez, K Samuels, S Walters, E Mieras, LA Paganessi, C Seong, ES Rich, **HC Fung**, and KW Christopherson

Update on a Prospective Study Evaluating the Safety and Efficacy of Combination Therapy with Fludarabine, Mitoxantrone and Rituximab Followed by Yttrium-90 Ibritumomab Tiuxetan and Maintenance Rituximab as Front Line Therapy for Patients with Indolent Lymphomas, R Karmali, M Kassar, AM Jimenez, P Venugopal, JM Shammo, **HC Fung**, RA Bayer, TM O'Brien, and SA Gregory:

Mocetinostat (MGCD0103), An Isotype-Selective Histone Deacetylase (HDAC) Inhibitor, Produces Clinical Responses In Relapsed/Refractory Hodgkin Lymphoma (HL): Update From a Phase II Clinical Study, Anas Younes¹, R. Gregory Bociek², John Kuruvilla³, Pierre Laneuville⁴, **Henry C. Fung**⁵, Michel Drouin⁶, Tracy Patterson⁶, Jeffrey M. Besterman⁶ and Robert E. Martell⁷

Recently opened clinical trials:

BDP-GVHD-03 - A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study of the Safety and Efficacy of Orbec® (Oral Becomethasone 17,21-Dipropionate) in Conjunction with Ten Days of High-Dose Prednisone Therapy in the Treatment of Patients with Gastrointestinal Graft VS. Host Disease

BMT CTN Protocol 0701 -- Phase II Trial of Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma Beyond First Complete Response

Publications and Clinical Trials Continued

Recently opened clinical trials:

A Phase II/III Randomized, Multicenter Trial Comparing Sirolimus plus Prednisone, Sirolimus/ Extracorporeal Photopheresis plus Prednisone, and Sirolimus/Calcineurin Inhibitor plus Prednisone for the Treatment of Chronic Graft-versus-Host Disease

A Multi-Center, Randomized, Double Blind, Phase III Trial Evaluating Corticosteroids with Mycophenolate Mofetil vs. Corticosteroids with Placebo as Initial Systemic Treatment of Acute GVHD

High Dose Chemotherapy with Autologous Stem Cell Rescue for Aggressive B Cell Lymphoma and Hodgkin Lymphoma in HIV-infected Patients).

A Phase II Study Evaluating the Safety and Efficacy of TXA127 in the Acceleration of Platelet Engraftment Following Autologous Peripheral Blood Stem Cell (PBSC) Transplant in Patients with Hodgkins Lymphoma or Non-Hodgkins Lymphoma undergoing Limited Re-infusion of CD34+Cells

A randomized, double blind, placebo controlled multi-center study of panobinostat for maintenance of response in patients with Hodgkin's lymphoma who are at risk for relapse after high dose chemo and autologous stem cell transplant. (PATH Study)

A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multicenter Clinical Trial to Study the Safety, Tolerability, Efficacy, and Immunogenicity of V212 in Recipients of Autologous Hematopoietic Cell Transplants (HCTs)

An Open-Label, Dose-Escalation, Multicenter Phase 1/2 Study of KW-2478 in Combination with Bortezomib in Subjects with Relapsed and/or Refractory Multiple Myeloma

BMT CTN 0702 A Trial of Single Autologous Transplant with or without Consolidation Therapy versus Tandem Autologous Transplant with Lenalidomide Maintenance for Patients with Multiple Myeloma

BMT CTN 0902 - Phase III Randomized, Multicenter Trial Testing Whether Exercise or Stress Management Improves Functional Status and Symptoms of Autologous and Allogeneic Recipients.