16TH INTERNATIONAL CORD BLOOD SYMPOSIUM

THURSDAY - JUNE 14, 2018

7:00 AM – 5:30 PM

Registration

7:15 AM – 8:15 AM

Breakfast with Exhibitors

8:30 am – 10:00 am

Welcoming Remarks and Keynote: Novel Therapies and the Regulatory Challenges They Bring

Chairs:

Karen Ballen, MD
Director, Stem Cell Transplant
University of Virginia

Donna Regan, MT(ASCP)SBB
SSM Cardinal Glennon Children's Hospital

8:30 am - 9:00 am

Regenerative Medicine Advanced Therapy (RMAT)
Wilson Bryan, MD
Director, Office of Tissues and Advanced Therapies
FDA / CBER
The 21st Century Cures Act ("Cures Act") defines "regenerative medicine therapy" (RMT) as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products. In November 2017, the FDA Center for Biologics Evaluation and Research (CBER) issued a draft guidance (Expedited Programs for Regenerative Medicine Therapies for Serious Conditions) which states that gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues may meet the definition of a RMT. In accordance with Section 3033 of the Cures Act, an RMT may qualify for designation as a regenerative medicine advanced therapy (RMAT). RMAT designation is an expedited program to facilitate the development of RMTs. The RMAT designation program has been administered by CBER's Office of Tissues and Advanced Therapies (OTAT). This presentation will describe the criteria to qualify for RMAT designation and will review the OTAT experience with RMAT applications.

9:00 am - 930 am

Gene Therapy for Hemoglobinopathies

Mark Walters, MD
Director, BMT Program
UCSF Benioff Children's Hospital, Oakland
Session Description: To come

9:30 am - 10:00 am

Unproven Therapies: From Do It Yourself Gene Editing to Stem Cell Tourism

Leigh Turner, PhD
Associate Professor
University of Minnesota

Over the last decade, health researchers and journalists have investigated "stem cell tourism" to clinics located in such countries as China, India, Mexico, Thailand, and the Ukraine. Social scientists, bioethicists, and other scholars have analyzed and critiqued the frequently misleading marketing claims made by such businesses. More recently, empirical studies have found hundreds of U.S.-based clinics selling unproven and unlicensed stem cell-based interventions. U.S. businesses engaged in direct-to-consumer marketing of putative stem cell treatments typically do not promote licensed medical products or advertise stem cell procedures that fall within the current scope of evidence-based medical practice. Their commercial and clinical practices prompt troubling concerns about patient safety, the use of "hope" to sell unproven stem cell interventions, the gap between the current state of stem cell research and the claims clinics use to sell supposed stem cell therapies, and the inadequate oversight provided by federal and state regulatory bodies. These businesses have proliferated to such an extent that the U.S. is now a major contributor to the global marketplace for unproven stem cell interventions. This presentation will provide an empirical analysis of the contemporary U.S. direct-to-consumer marketplace for stem cell interventions and explore ethical issues related to the proliferation of U.S. clinics selling purported stem cell treatments. The presentation will also review the U.S. federal regulatory framework for stem cell-based medical interventions, summarize recent enforcement activity by the FDA, and examine several lawsuits filed by former patients of U.S. stem cell clinics. The talk will explore how the U.S. has shifted from being a point of departure for patients engaging in "stem cell tourism" to becoming a country with a large domestic marketplace for unproven stem cell products. The presentation will end by considering how this market might expand and reshape itself in response to deregulatory pressures, public mistrust of scientific institutions and regulatory bodies, and the emergence of "biohacking" and "DIY gene editing."

10:00 am - 10:30 am

Refreshment Break with Exhibitors

10:30 am – 12:00 pm

Outcomes of Cord Blood Transplant

Session Description: To come

10:30 am - 11:00 am
"Best of European Studies" - Highlights from EBMT and Eurocord
Annalisa Ruggeri, MD, PhD
Session Description: To come

11:00 am - 11:30 am
The Application of Umbilical Cord Blood Transplantation in Pediatric Primary Immunodeficiency Disease
Xiaowen Zhai, MD
Session Description: To come

11:30 am - 12:00 pm
HHV-6 Prophylaxis with Foscarnet: Implications for Cord Blood Transplantation
Claudio Brunstein, MD, PhD
University of Minnesota
Session Description: To come

12:00 pm – 1:30 pm

Lunch with Exhibitors

1:30 pm – 3:00 pm

Novel Cord Blood Derived Cellular Therapies and Their Clinical Applications

Chair:

David McKenna, MD

University of Minnesota

Session Description: To come

1:30 pm - 2:00 pm
Large Scale Bioreactor Generated Expansion of Cord Tissue Derived MSCs for Clinical Use

Qasim Rafiq, PhD
Session Description: To come

2:00 pm - 2:30 pm
Cord Blood Derived NK Cells for Multiple Myeloma

Nina Shah, MD
Session Description: To come

2:30 pm - 3:00 pm

Cord Blood Derived Virus Specific T Cells for the Treatment of Infections Post Allogeneic Stem Cell Transplantation

Patrick Hanley, PhD

Director, Cellular Therapy Laboratory

Children's National Health System

Session Description: Cord blood transplantation is an alternative method of stem cell transplantation that can be curative for some malignancies and genetic disorders. However, the necessary conditioning associated with the transplant renders patients susceptible to viral infections, such as those from CMV, EBV, and adenovirus. Our group and others have shown that virus-specific T cells are an attractive option for treatment or prophylaxis of viral infection, but the expansion of virus-specific T cells is challenging when the donor is not seropositive for the virus. Here we will discuss a new approach to expanding virus-specific T cells from the naive T cell population that is predominant in cord blood. We will discuss new methods of expanding these cells as well as their clinical safety and potential efficacy.

3:00 pm – 3:30 pm

Refreshment Break with Exhibitors

3:30 pm – 5:00 pm

Simultaneous Session A - Cord Blood Expansion: Clinical Trials and Outcomes

Chair:

John Miller, MD, PhD

Vice President and Senior Medical Director

NMDP

Session Description: To come

3:30 pm - 4:00 pm

Phase II Trials of MGTA-456 - Results of Ex Vivo Expanded Hematopoietic Stem Cells from a Single Cord Blood Unit

John Wagner, MD

Professor *University of Minnesota*

Umbilical cord blood (UCB) has been limited by the low number of CD34+ cells, resulting in prolonged periods of cytopenias and high risk of graft failure, restricting its widespread application. MGTA-456, the hematopoietic stem cell product after cord blood CD34+ cells are placed in expansion culture for 15 days with an aryl hydrocarbon receptor antagonist and SCF, Flt-3L, IL-6 and TPO. In a prior Phase 1/2 safety study, 18 patients received MGTA-456, its accompanying $CD34^{neg}$ fraction and a larger, unexpanded UCB unit. All patients engrafted at a median of 14.5 days (range, 7-23), significantly faster than similarly treated historical controls ($p<0.01$). Based on these results, MGTA-456 was evaluated as a stand-alone graft after myeloablative conditioning (MAC) or non-myeloablative conditioning (NMAC). Twenty patients with high-risk hematologic malignancy were enrolled and 18 were treated. The presentation

will focus on the results of the trials to date and future implications for the future of UCB transplantation.

4:00 pm - 4:30 pm

Nicord Single Unit Expanded Cord Blood Transplantation - Final Results

Mitchell Horwitz, MD

Session Description: To come

4:30 pm - 5:00 pm

The UM171 Cord Blood Expansion Trial: Working Towards the Ideal Graft

Sandra Cohen, MD, FRCP(C)

Maisonneuve Rosemont Hospital-University of Montreal

Cord blood (CB) transplants are hampered by low cell dose and high transplant related mortality (TRM). UM171, a novel, potent agonist of hematopoietic stem cell (HSC) self-renewal could solve this hindrance, allowing for CB's lower risk of chronic GVHD and relapse to prevail. Hence, we initiated a trial to test the safety and efficacy of UM171 expanded CB (eCB). The procedure was designed to be clinically viable.

Patients (patients) received an ablative conditioning. On day(D)-7, CB was thawed and $CD34^+$ selected. The $CD34^-$ lymphocyte containing fraction was cryopreserved and infused on D0. The $CD34^+$ cells were placed in a closed culture system supplemented daily with UM171-containing media until D0, when cells were washed and infused. This culture system allowed for small culture volumes (median 0.6 liter), saving cost and labor.

Between 7/16-1/18, 17 adults were transplanted with a single UM171 eCB and 1 patient received a double CB and engrafted 100% with the UM171 CB (median age 44 years, range 19-63). Results are described for these 18 patients. Median BMT comorbidity index was 2 (0-5). Four patients had already failed an allogeneic transplant and 1 patient had refractory relapsed ALL. Net CD34 expansion was 34 fold. Median 1st day of 100 and 500 neutrophils were D+9 and D+18, respectively. Achieving 100 neutrophils was faster than expected and cell dose independent, suggesting that clinically meaningful expansion of an early repopulating myeloid progenitor is at saturation even with small CBs. In contrast, attaining 500 neutrophils was accelerated but dependent on infused $CD34^+$ dose. Importantly, patients derived clinical benefit much earlier than engraftment of 500 neutrophils. For example, and when compared to our patients who received the same conditioning regimen with peripheral blood or marrow, eCB patients were free of fever much earlier (D+7 vs D+15 $p<.001$). Moreover, hospitalization was reduced by 11 days when compared to our non UM171 CB transplants. Furthermore, with a median follow up of 10 months (range 2-20), there has been no CMV disease, no PTLD, only 1 grade 3-4 acute GVHD, no moderate or severe chronic GVHD, 1 TRM from alveolar hemorrhage and only 1 relapse in a group of high risk diseases. Progression free survival (PFS) and GVHD-free and relapse-free survival (GRFS) are at 85 and 75%, respectively at 10 months. Full donor chimerism was achieved in all cell subsets.

These results favorably compare to those of other expansion trials which utilize much larger (up to 20L) and longer (up to 21 days) cultures. Moreover, and in contrast to others, we have already initiated our dose reduction study with smaller, better HLA matched CBs, proven to reduce TRM. We offer 3 hypotheses as possible contributors for these favorable outcomes in our very high risk patient group: i)

100 neutrophils, which are attained much earlier at D+9, provide significant defense against infection, ii) the graft contains a significant proportion of dendritic and mast cell precursors which may promote immunomodulation, reduce gut bacteria translocation and lower relapse risk and iii) because cell dose requirements were lower, more than half of patients received a better HLA matched CB. In conclusion, this 1st trial positions UM171-expanded CB as a very promising HSC source and if results are confirmed in larger multicenter studies, UM171 CB could become the graft of choice.

3:30 pm – 5:00 pm

Simultaneous Session B - The Corporate Match: Connecting Available Units from Cord Blood Banks with Their Industry Partner End Users

Chair:

Donna Regan, MT(ASCP)SBB

SSM Cardinal Glennon Children's Hospital

This session will serve as a 'mixer' where facilitators will discuss topics such as the types of raw materials available for research and commercial development, the development of donor consents, and the benefits of synergies - acknowledgement, credibility and profit sharing.

Moderators:
Terri Tibbot, MS, CTBS
Life Line Stem Cell

Georgina Michael, MSN, RNFA, FNP-BC, CWCN
Osiris Therapeutics, Inc.

5:30 pm – 7:00 pm

Welcome Reception and Poster Viewing

FRIDAY - JUNE 15, 2018

7:00 AM – 5:30 PM

Registration

7:00 AM – 7:45 AM

Breakfast with Exhibitors *(Garden Pavilion)*

8:00 am – 9:30 am

Controversies in Cord Blood Transplantation: Expert Perspectives

Chair:

Karen Ballen, MD

Director, Stem Cell Transplant

University of Virginia

In this session, currently controversial topics in cord blood transplantation will be discussed by two experts discussing opposing perspectives. Following each topic, an energetic discussion will ensue as the audience participates in the debate.

The first session will highlight whether high resolution typing (Mary Eapen, MD, MS) vs CD34+ Enumeration (Joanne Kurtzberg, MD) is important in cord blood unit choice. At 9:15 am, Karen Ballen, MD and Claudio Brunstein, MD, PhD will discuss the role of HLA matching at the C Locus in cord blood donor unit selection.

8:00 am - 8:45 am

High Resolution Typing Vs CD34+ Enumeration in CB Unit Choice

Mary Eapen, MD, MS

Joanne Kurtzberg, MD

Session Description: To come

8:45 am - 9:30 am

Is HLA Matching at the C Locus Necessary?

Karen Ballen, MD

Claudio Brunstein, MD, PhD

Session Description: Over 40,000 unrelated cord blood transplants (UCBT) have been performed worldwide. There was an early understanding that other features besides the traditional Human Leukocyte Antigen (HLA) typing used for adult volunteer donors were important for transplant success. For example, the importance of a higher cell dose as a critical factor for engraftment and survival was recognized in the 1990s. An advantage of UCBT is that the patient and the UCB unit do not need to be a "perfect" match, likely due to the naïve immune system of the newborn baby. HLA-C is recognized as an important determinant of relapse and graft vs host disease in adult volunteer donor unrelated transplants. But the importance of matching at HLA- C is still under investigation in UCBT. Preliminary data in both the myeloablative and reduced intensity setting suggest a benefit to choosing an HLA-C matched unit, but this practice has not been widely adapted. In addition, the importance of HLA-C

matching compared to other factors when selecting an UCB unit is unclear. Is it better to match at HLA-C than HLA-DR? Should one choose an UCB unit with a lower total nucleated cell dose to achieve a match at HLA-C? In this session, we will try to address these important but controversial issues.

9:30 AM – 10:00 AM

Transforming Outcomes for Pediatric Neurologic Diseases with Cord Blood and Cord Tissue Therapies
(International Ballroom)

Moderator: **Joanne Kurtzberg, MD**, Director*, Carolinas Cord Blood Bank*

10:00 am – 10:30 am

Refreshment Break with Exhibitors

10:30 am – 12:00 pm

Workshop A: Selecting Cord Blood Units

Chair:

Andromachi Scaradavou, MD,

New York Blood Center, National Cord Blood Program

Session Description: To come

10:30 am - 11:00 am
Selecting Optimal Cord Blood Units: Limitations of Cell Dose

Martin Maiers

Session Description: Hematopoietic stem cell transplantation (HCT) is a potentially lifesaving therapy for blood cancers and other diseases. For patients without a suitable related donor, unrelated-donor registries of adult volunteers and banked umbilical cord-blood units provide potential sources of donors. Umbilical cord transplantation has several advantages including lack of adverse effects on the donor, near-immediate availability and lower risks of acute and chronic graft-versus-host disease, even with donor-recipient HLA-disparity. The main disadvantage is the low absolute number of cells in each unit, often insufficient for engraftment and timely recovery of hematopoiesis in adults. Consequently, cell dose is often the prime driver of unit selection and HLA matching criteria are much less stringent than used for adult unrelated donor HCT. Most cord blood transplantations are mismatched for one or two HLA A, B and DRB1 loci, using only intermediate resolution typing for HLA A and B. HLA C is usually not considered. However, recent data from the CIBMTR suggest that outcomes are substantially better and transplant-related mortality rates very low (~5%) when cord blood units are matched with recipients for HLA-A, B, C and DRB1 (using high resolution typing for all loci) are selected.[1,2] We sought to determine the likelihood of finding a suitable 6-8 of 8 HLA-matched cord blood unit for patients in the United States, given the current available inventory, and the potential impact of technologies that would allow smaller than currently acceptable units to be used successfully.
Using human HLA data from the NMDP cord-blood-unit registry, we built population-based genetic models for 21 U.S. racial and ethnic groups to predict the likelihood of identifying a cord-blood unit for patients in each group. The models incorporated the degree of HLA matching and cord-blood-unit pre-

freeze total nucleated cell (TNC) dose. We also calculated models that assumed that cord-blood-unit TNC dose was not a limitation. Our models indicated that currently, 81.8% of patients will identify a suitably-sized cord blood unit that is matched at high-resolution for 6-8 of 8 HLA A, B, C, DRB1 loci. This likelihood varies by patient race and ethnicity, from 49.4% to 87.4% patients. If cell dose were not an issue, these percentages increase with 97.4% of patients overall predicted to have a 6-8 of 8 HLA matched unit. Considering patient race/ethnicity, the likelihood is 98.9% for European Caucasians, 94.5% for Hispanics, 93.3% for Asian or Pacific Islanders and 87.1% for African Americans, for children and adults. The impact of TNC dose (and the potential impact of agents allowing cord blood units with smaller TNC doses to be used) is greatest for adults and people of color, particularly African Americans. Strategies to facilitate successful engraftment using lower cell dose units could increase the numbers of patients who could receive an optimally HLA-matched cord blood unit, with subsequent improvements in outcomes.

11:00 am - 11:30 am

Adoptive Immunotherapy with Cord Blood Grafts Targeting Shared IPA and/or NIMA

Andromachi Scaradavou, MD

New York Blood Center, National Cord Blood Program

Session Description: To come

11:30 am - 12:00 pm

Update on 10-CBA Protocol: An IND Study

John Miller, MD, PhD

Vice President and Senior Medical Director

NMDP

Session Description: To come

10:30 am – 12:00 pm

Workshop B: Translational Projects using Placental Derived Cells

Chair: **Naynesh R. Kamani, MD**

Formerly, Vice President, Center for Cell Therapies and Research

AABB

Session Description: To come

10:30 am - 11:00 am

CRISPR/Cas9 Gene Editing: A Primer

Matthew Porteus, MD, PhD

Session Description: To come

11:00 am - 11:30 am

Exosomes of Placental Derived MSC Stimulate Angiogenesis

Jan Nolta, PhD

Professor, Director

University of California Davis

Session Description: To come

11:30 am - 12:00 pm

Improvement of Enzyme Activity in Vitro of GALNS Deficient Fibroblasts by Umbilical Mesenchymal Stem Cell-Mediated Microvesicles

Adriana Montano, PhD

Associate Professor

Saint Louis University

Session Description: To come

12:00 pm – 1:30 pm

Lunch with Exhibitors

1:30 pm – 2:45 pm

Workshop C - Top 5 Manufacturing Challenges in Cord Blood Banking

Chair:

Rebecca Haley, MD

Facilitators:

Andromachi Scaradavou, MD

New York Blood Center, National Cord Blood Program

Mike Halpenny, MLT (CMLTO)

Canadian Blood Services

Rebecca Haley, MD

Bloodworks Northwest

This workshop will explore the top 5 Manufacturing challenges. Topics include:

- Releasing products that are out of specifications, especially conditions that require release under IND instead of full licensed release (USA), or special release (Canada)
- Post-thaw testing options, best practices, and non-destructive testing methods
- Potency considerations for the inventory currently available under NMDP, patient size considerations
- Outsourcing production or part of the manufacturing – necessary contracts and arrangements
- GMP manufacturing for cord blood – process vs facility

1:30 pm – 2:45 pm

Workshop D - National Cord Blood Inventory: Crisis or Opportunity?

Chair: **Brian Freed, PhD**

Session Description: To come

1:30 pm - 1:55 pm

HRSA - The RAND Report: Response and Next Steps

Karen Ballen, MD

Director, Stem Cell Transplant

University of Virginia

Session Description: The US government began to federally fund umbilical cord blood (UCB) banks in 2005 to create a nationwide inventory of high quality and genetically diverse UCB units. In 2017, the US Department of Health and Human Services commissioned the RAND Corporation to evaluate the economics and sustainability of the National Cord Blood Inventory (NCBI). The key findings from the RAND Corporation included an assessment of the decline in the number of UCBT performed, and the recognition that some of the 19 US public cord blood banks may need to limit collections, close completely, or find new financial partners. The report suggests that the current structure of the NCBI, which rewards the quantity of UCB units banked, may limit the quality (measured by high total nucleated cell count) of the UCB units that are available for transplantation. The RAND report highlighted that the value of a public cord blood system outweighed the costs involved and that UCBT was particularly important for certain populations, not well served with other donor sources. In this session, we will review the findings of the RAND report and discuss its implications for the cord blood community.

1:55 pm - 2:20 pm

The Role of the Cord Blood Bank in Developing New Products

Brian Freed, PhD

Session Description: To come

2:20 pm - 2:45 pm

Consolidation of Public Cord Blood Banks: A Case Study

Donna Regan, MT(ASCP)SBB

SSM Cardinal Glennon Children's Hospital

Session Description: To come

2:45 pm – 3:15 pm

Refreshment Break with Exhibitors

3:15 pm – 4:15 pm

Oral Abstract Presentations

Chair & Moderator:

Kate S. Brown, PhD

Scientific Director, Research and Development

CBR Systems, Inc.

Session Description: To come

4:15 pm – 5:30 pm

Workshop E - Delayed Clamping: Balancing Product Quality and Donor Safety

Chair:

Kate Girard, RN, MSN

Director of Medical and Scientific Affairs

ViaCord, a Perkin Elmer Company

Session Description: To come

4:15 pm - 4:40 pm

Reconciling Procurement Practice with Clinical Recommendations (ACOG and AAP)

Rebecca Haley, MD

Bloodworks Northwest

Session Description: To come

4:40 pm - 5:05 pm

Impact of Delayed Clamping on Public Cord Blood Banking

Andromachi Scaradavou, MD

New York Blood Center, National Cord Blood Program

Session Description: To come

5:05 pm - 5:30 pm

Delayed Clamping and Its Impact on Product Volume and Evaluation of Collection Devices

Kate Girard, RN, MSN

Director of Medical and Scientific Affairs

ViaCord, a Perkin Elmer Company

Session Description: To come

4:15 pm – 5:30 pm

Workshop F - New Models for Public/Private Partnerships in Hematopoietic Stem Cell Banking

Chair:

Mrinalini Chaturvedi, MBBS, MD, MBA, PGDMLE

Session Description: To come

4:15 pm - 4:40 pm

Procurement of HSCs from Deceased Donor Bone Marrow: Implications for Minority Recipients

Prakash Rao, PhD, MBA, FACHE, HCLD

VP, Diagnostics & Research Operations and Director, Transplant Laboratory

NJ Sharing Network

Session Description: To come

4:40 pm - 5:05 pm

Session Description: To come

5:05 pm - 5:30 pm

Redefining Cord Blood Banking: Charting New Paths in Asia

Mrinalini Chaturvedi, MBBS, MD, MBA, PGDMLE

Session Description: To come

Saturday - June 16, 2018

7:00 AM – 7:45 AM

Networking Breakfast *(Garden Pavilion)*

7:00 AM – 10:30 AM

Registration

8:30 am – 10:30 am

Regenerative Medicine Applications of Cord Blood/Tissue Derived Therapies

Chair:

Charles Cox, MD

UTHealth

Session Description: To come

8:30 am -9:00 am
Cord Blood Transplantation in HIV Infected Patients Using CCR5 -/- Units
Koen van Besien, MD, PhD
Weill Cornell Medicine
Session Description: To come

9:00 am – 9:30 am
Cord Blood Derived Cells for the Treatment of Hypoplastic Left Heart Syndrome

Susana Cantero Peral, MD, PhD

Associate Consultant

Mayo Clinic
Session Description: To come

9:30 am – 10:00 am
Cord Tissue Derived MSC for the Treatment of Lupus in Adults

Gary Gilkeson, MD
Session Description: To come

10:00 am – 10:30 am
Cord Blood for Treatment of Traumatic Brain Injury

Charles Cox, MD

UTHealth
Session Description: To come

10:30 am – 11:00 am

Refreshment Break

11:00 am – 12:30 pm

Regenerative Medicine Applications of Perinatal Tissue Derived Therapies

Chair:

Frances Verter, PhD

Founder & Director

Parent's Guide to Cord Blood Foundation

Session Description: To come

11:00 am - 11:30 am

Competing Clinical Trials of Expanded Cord Blood

Fran Verter, PhD

Founder & Director

Parent's Guide to Cord Blood Foundation

Session Description: To come

11:30 am - 12:00 pm

Cryopreserved Placental Membrane for Wound Care

Georgina Michael, MSN, RNFA, FNP-BC, CWCN

Session Description: To come

12:00 pm - 12:30 pm

Perinatal Cell Therapy for the Treatment of Inflammatory Lung Diseases

Oula Khoury, MS (PhD Candidate)

Wake Forest Institute for Regenerative Medicine

Session Description: To come

12:30 pm – 2:00 pm

Networking at Noon

Lunches will be available for attendees to take with them or meet with colleagues at the conclusion of the Symposium.

End of Program