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Testimony Before the U.S. House of Representatives House Energy and Commerce Committee Health Subcommittee

"Improving Access to Care: Legislation to Reauthorize Key Public Health Programs"

July 29, 2020

Introduction:

Chairwoman Eshoo, Ranking Member Burgess, and members of the Subcommittee, I appreciate the opportunity to share my thoughts on H.R. 4764, the Timely ReAuthorization of Necessary Stem-cell Programs Lends Access to Needed Therapies Act of 2019, better known as the TRANSPLANT Act.

My name is Joanne Kurtzberg, and I currently serve as the President of the Cord Blood Association (CBA). The CBA is an international, non-profit organization that promotes both public and family cord blood banking, with the objectives of saving lives, improving health and changing medicine. Our priorities are advocacy, quality products and services, market expansion, research and development, and public and professional education. CBA members include public and family cord blood banks as well as health care providers in the cord blood community and their patients and families.

In addition to serving as the President of CBA, I also serve in multiple roles at Duke University. I am a Distinguished Professor of Pediatrics and Professor of Pathology in the School of Medicine, and Director of the Marcus Center for Cellular Cures, which is a joint Center of the School of Medicine and the Pratt School of Engineering. I also established and direct the Pediatric Blood and Marrow Transplant Program and am Co-Director of the Stem Cell Laboratory. Finally, I am the Director of the Carolinas Cord Blood Bank, which is an FDA licensed public cord blood bank and a member of the National Cord Blood Inventory (NCBI) of the CW Bill Young Cell Transplantation Program. I have dedicated my professional career to cord blood research, banking and transplantation.

Both the CBA and Duke University School of Medicine strongly support passage of the TRANSPLANT Act. I want to thank both Congresswoman Doris Matsui, Congressman Chris Smith, and Congressman Gus Bilirakis for their leadership on the introduction of the legislation to reauthorize this important program, specifically H.R. 4764, the TRANSPLANT Act and H.R. 3520, the Stem Cell Therapeutic and Research Reauthorization Act of 2019.

I also want to acknowledge this Committee's unwavering bipartisan commitment to the creation and support of public cord blood banks, which began when the bill was first introduced in 2005. The original Stem Cell Therapeutic and Research Act of 2005 reflected a compromise between Congress and the key stakeholder groups deeply interested in establishing cord blood banks for public use. This legislation not only reauthorized the National Marrow Donor Program (NMDP) but also created a national network of public cord blood banks. The law also provides health care professionals the ability to search for unrelated bone marrow donors and cord blood units through a single electronic point of access, the "Be the Match" registry, which is operated by NMDP.

All of us working on the 2005 bill had one goal in mind – to expand patient access to the best therapies possible. We worked together to get this legislation approved by Congress and signed into law by the President. The 2005, 2010, and 2015 bills were approved by both the House and the Senate with overwhelming support.

In the House, the late Congressman Bill Young, Congressman Chris Smith and Congresswoman Doris Matsui played important roles – without their leadership, we would not be where we are today. All of us who have worked on this program for the last 15 years are so grateful for your long-standing dedication, and we look forward to working with all of you again this year.

The bill that we are discussing today reauthorizes both the NCBI Program and the C.W. Bill Young Cell Transplantation Program from Fiscal Year 2021 through Fiscal Year 2025. The NCBI would be reauthorized at $23 million each year and the C.W. Bill Young Cell Transplantation Program would be reauthorized at $30 million each year. Both programs have made a tremendous difference in the lives of thousands of patients, as I will discuss in greater detail, beginning first with a description of the National Cord Blood Inventory.

The National Cord Blood Inventory

The National Cord Blood Inventory (NCBI) was created in 2006 as part of the C.W. Bill Young Cell transplantation Program after passage of the Stem Cell Therapeutic and Research Act of 2005. The original and overriding goal of the C.W. Bill Young Program was to provide access to transplantation for patients lacking a related donor through increasing the available donor pool thereby increasing the number of unrelated donor blood stem cell transplants performed each year. This goal was approached through a series of contracts from HRSA to the National Marrow Donor Program (NMDP) and to selected high quality public cord blood banks in the USA. The goals of the NCBI were to create a network of cord blood banks and make available high-quality, diverse umbilical cord blood units, to add at least 150,000 new cord blood units to the registries inventory, and to make additional cord blood units available for research. The C.W. Bill Young Program's additional cord blood priorities also included the establishment of the Cord Blood Coordinating Center (CBCC) to provide financial support to NCBI banks to make cord blood units more rapidly available through the Program. Contracts for NCBI are awarded through and negotiated by the Health Resources and Services Administration (HRSA). The contract for the CBCC is competed through a Request for Proposal (RFP) process from HRSA and is currently and historically awarded to the NMDP.

Cord blood, or the baby's blood remaining in the placenta or afterbirth, can be collected after the birth of the baby without risk to the mother or baby. In fact, in the past, cord blood was routinely discarded as medical waste. With the discovery that cord blood contained important stem cells of the blood as well as other types of therapeutic cells, collection of cord blood for banking and later use in medical therapies is now common practice. Cord blood can be collected after a vaginal or cesarean section delivery. Generally collections are performed within 10 minutes of the birth of the baby. After collection, cord blood is transported to a processing laboratory where it is qualified, volume and red blood cell reduced, and frozen at ultra-cold temperatures for long-term storage. Today, we know that cord blood units can be stored for over 25 years and successfully used for transplantation of patients with blood cancers and certain genetic diseases. Each cord blood unit is tested to ensure that the proper numbers of cells were collected, that the cells are alive, that the cells are sterile and that the cells are potent (capable of restoring the blood forming system in a patient whose system was destroyed by treatment and or disease). Mothers donating their baby's cord blood are screened to be sure they do not have any infectious or genetic diseases that can be transmitted through the blood. Public cord blood banks recruit and educate mothers to donate their baby's cord blood so that it can be distributed to patients in need of a donor for blood stem cell transplantation. Qualified cord blood units are listed on the NMDP "Be the Match" registry and distributed through the NMDP from banks to transplant centers for use in patients.

A goal of adding 150,000 high quality unrelated donor cord blood units to the national registry was established by the original legislation. This number was based on assumptions about HLA (Human Leukocyte Antigens) matching that would allow for 50% of patients to identify a 5/6 matched donor, and 90% to identify a 4/6 matched donor. To support accrual of cord blood units towards this goal, the NCBI was authorized to receive approximately $90 million during the first 5-year authorization cycle; however, the amount appropriated to this program has been woefully inadequate. It is my hope that the current and future congressional appropriations process will recognize the importance of fully investing in the NCBI program to ensure the collection of the largest and most diverse units.

Cord Blood Licensure

The original legislation also called for the establishment of guidelines for licensure of unrelated donor cord blood banks by the Food and Drug Administration (FDA). Multiple hearings occurred and draft guidance for licensure was issued and finalized. To date, eight of the NCBI banks have been granted licenses from FDA. The process of obtaining and maintaining licensure has been challenging for the public banks to date. Many of the regulations, created for drug manufacturing, are not easily applied to manufacturing of cord blood units, particularly when each cord blood unit represents a 'batch' or a lot of one. Requirements for an expiration date, for requalification of materials FDA approved for cord blood manufacturing, timelines for approvals of manufacturing changes and other aspects of the current FDA regulations are seen by some as stifling innovation and progress in the field. Furthermore, licensure has greatly increased the costs associated with public cord blood banking, diverting limited resources from the recruitment and collection of cord blood donors and banking of new cord blood units.

Brief history of cord blood banking and transplantation

In the mid 1980s, Hal Broxmeyer and other scientists showed that cord blood contained high numbers of young blood stem cells. In fact, cell for cell, cord blood was highly enriched for these blood forming stem cells as compared to bone marrow, the traditional source of these types of cells. Shortly after these observations were reported, a cord blood transplant was planned for a five year old boy with Fanconi Anemia (a genetic disease affecting the blood and leading to bone marrow failure, or leukemia, and death in the first decade of life) under my care at Duke whose mother conceived a healthy child who was a full match to her brother. A team of physicians and scientists in New York City and at Duke arranged for the cord blood to be collected at the time of the baby's birth and later, for the transplant to be performed by Dr. Eliane Gluckman at L'Hospital St. Louis, in Paris, France. The transplant performed in 1988 was a success and paved the way for the field. The patient, named Matthew, is now nearly 36 years of age, working and living a healthy productive life. Importantly, he is fully engrafted with his baby sister's cord blood cells and as such, is living proof that cord blood contains blood stem cells that can repopulate the bone marrow (blood factory) and immune system for life.

After that transplant, others were performed between siblings, confirming the findings of the first transplant. In addition, these transplants, using cord blood, caused significantly less of a complication of transplantation called graft-versus-host disease (GVHD), which is a serious condition in which the donor cells attack the recipient. GVHD is a major barrier to the success of blood stem cell transplantation overall. Given that cord blood causes less GVHD, it was hypothesized that cord blood could be used in the unrelated setting and also that cord blood might not have to match as closely as bone marrow. This is important because there are many patients in need of a donor for transplantation who cannot find a fully matched donor.

In 1992, the first unrelated cord blood bank was created at the New York Blood Center by Dr. Pablo Rubinstein and with the support of the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). I established a pediatric blood and marrow transplant program at Duke in 1990 and collaborated with Dr. Rubinstein, agreeing to use cord blood units from his bank for transplantation. In 1993, we performed the first unrelated donor cord blood transplant in the world at Duke in a young child with refractory leukemia. The transplant engrafted (grew in the bone marrow), in spite of the fact that the cord blood unit and the patient matched at only four of six required locations. Over the next few years, additional transplants were performed at Duke and in other transplant centers, establishing the benefits of cord blood for use in blood stem cell transplantation to treat patients with blood cancers, bone marrow failure, congenital immune deficiencies, certain inherited metabolic diseases and hemoglobinopathies (sickle cell anemia and thalassemias).

In 1996, the NHLBI was funded through Congress to establish additional public cord blood banks and to study the applications of cord blood donors in blood stem cell transplantation. They established and issued RFPs for the COBLT (Cord Blood Transplantation Program), a program which funded the establishment of three additional public banks in the United States and five multicenter prospective clinical trials designed to test the potential benefits of cord blood as a donor for unrelated transplantation. I, on behalf of Duke, applied for and was awarded one of the

three banking contracts and established the Carolinas Cord Blood Bank in 1997. I was also one of the principle investigators (PIs) for the COBLT clinical transplantation studies and served on the steering committee for both the banking and transplantation projects. This steering committee established standards for cord blood banking and the initial guidelines for the use of cord blood in blood stem cell transplantation. Over time, innovative models for kit donations, automation of processing techniques, assays for cord blood viability and potency have been developed.

Early experiences with cord blood transplantation demonstrated that not all cord blood units contained enough cells to transplant a single adult. Establishment of a minimal effective cell dose based on the weight of the recipient was determined for transplantation of patients receiving preparative therapy that destroyed their bone marrow and immune systems (myeloablative conditioning). It was also recognized that the amount of cord blood that could possibly be collected from a single placenta was limited and that the majority of collected units were too small for the transplantation of larger children and adults. This led investigators at the University of Minnesota, Drs. John Wagner and Juliet Barker, to pilot the use of two cord blood units for a single transplant in adults in 2005. This approach was successful and increased access to cord blood transplantation for larger children and adults. However, it also increased the costs of cord blood transplantation because two cord blood units had to be utilized for one transplant.

Between 2005 and 2010, the double cord blood transplant approach was tested in a multicenter, phase III trial in pediatric patients with acute leukemia conducted by the Blood and Marrow Transplant Clinical Trials Network (BMT-CTN). John Wagner and I were the PIs of this study, which showed that in children, one cord blood unit was sufficient for transplantation when the unit contained enough cells. In fact, children receiving two cord blood units had more GVHD than those receiving one unit. In adults, however, the practice of double cord blood transplantation continues, with increased GVDH and increased costs of transplantation.

Strategies to increase the numbers of cells provided by a single cord blood unit are the subject of active and ongoing scientific investigation. Ex vivo expansion (or expanding stem cells in the laboratory) before infusion to the patient is showing great progress. At least five promising technologies are currently undergoing testing in the clinic under INDs from FDA. One of these technologies has been proven to accelerate engraftment of cord blood in a recently completed phase 3 registration trial and a BLA for this technology is in preparation. These modified cord blood products engraft (or grow back) more rapidly after transplant as compared to unmodified cord blood. For example, average times to engraftment after a standard cord blood transplant range from 20-27 days. With ex vivo expansion, engraftment times have decreased form 25-35 days to 7-15 days. Additional technologies that improve homing of cord blood cells to the bone marrow are also being tested.

Today, cord blood is a standard graft source for unrelated donor blood stem cell transplantation, providing access to transplantation for patients who lack a matched related donor in their family or unrelated adult donor. The program has particularly met the needs of patients of minority ancestry, as they are less likely to find a fully matched donor. The lower incidence of GVHD is another advantage of this unique stem cell product. Emerging evidence also suggests that when a cord blood donor is used to transplant a patient with acute leukemia, relapse post-transplant is

lower than when other types of donor cells are utilized. Cord blood is also an important graft source for patients with sickle cell anemia, a disease which can be cured with blood stem cell transplantation.

However, there are challenges to the success of cord blood transplantation. Cord blood engrafts more slowly than bone marrow or adult cells, leading to longer hospitalizations for recipients of cord blood units. The immune system, which comes from a newborn baby, also recovers more slowly after a cord blood transplant compared to other sources. These obstacles can in part be addressed with transplantation of larger cord blood units. However, these units must also be racially diverse. Thus, there is a great need for larger, racially diverse units in the NCBI. Biological properties of blood stem cells vary by race. Specifically, blood from African American donors has fewer cells per volume than blood from Caucasian donors. Thus, to increase the size of cord blood units in the inventory while preserving ethnic and racial diversity, increased collections of cord blood units, particularly from minority births units, must be supported. Furthermore, the 150,000 unit target may be outdated today. Rather than targeting a specific number for the inventory, the largest and most diverse units should be targeted. As such, funding strategies should be readjusted to enable increased collections and banking of the largest, racially diverse units.

The potential of cord blood in cellular therapies and regenerative medicine

In addition to use in patients with malignant and genetic diseases, cord blood is showing enormous potential for use in the emerging fields of cellular therapies and regenerative medicine. Cord blood-derived vaccines against viruses and certain types of cancers are currently under development and in early phase clinical trials. Cells, manufactured from cord blood units, are being developed to boost recovery of the immune system, to prevent leukemic relapse, and to treat life-threatening opportunistic infections that develop in recently transplanted patients. Cells regulating autoimmunity (Regulatory T cells) are also in early clinical trials. These approaches, which often utilize cord blood banked in family banks, may help patients with Type I Diabetes, as well as other diseases.

We, and others, are developing uses for cord blood to treat acquired brain disorders. Over the past six years, we have initiated trials of autologous (the patient's own) cord blood in babies with birth asphyxia (hypoxic ischemic encephalopathy), cerebral palsy, hearing loss, and autism. These studies are showing promising results in conditions for which few treatments are available. We now realize that it will never be possible for all patients who might benefit from cord blood therapies to have access to their own cord blood. For this reason, we demonstrated that the use of donor cord blood was safe in adults with acute ischemic stroke. We then tested donor cord blood in children with autism and cerebral palsy and have recently completed phase 2 studies describing efficacy in these diseases. In addition, the infrastructure created by FDA licensed public cord blood banks has enabled procurement of GMP compliant source material for manufacturing of cord tissue MSCs and other non-hematopoietic cells that can be used to treat patients with a number of pro-inflammatory conditions including GVHD and complications of COVID-19 infections.

Summary

In summary, I have testified that cord blood holds enormous potential for use as a donor for blood stem cell transplantation, providing increased access to transplantation for patients unable to find a fully matching related or unrelated adult donor. Cord blood cord tissue cells are also extremely important for the emerging fields of cellular therapies and regenerative medicine. Cord blood must be harvested in a fashion that maintains sterility, protects against disease transmission, and promotes collection of large numbers of cells. Techniques for cord blood banking are well established, but there is a need to explore methods to recover more cells from each collection. Exciting advances in cord blood expansion technology are likely to reduce the risk of a cord blood transplant, extending its use to patients with chronic but serious diseases like Sickle Cell Anemia. Cord blood and derivative therapies can be utilized to treat children with brain injuries and show great promise for treatment of adults with stroke and other chronic and debilitating diseases.

The NCBI program has created a large inventory of high quality, racially diverse, unrelated donor cord blood units for use in patients needing a donor for blood stem cell transplantation. Continuation and refunding of the program is essential to continue to increase the number of units listed in the NCBI and also to increase the size and diversity of units banked. The potential for cord blood to treat additional serious and life-threatening diseases is just beginning to be realized. With these new applications, it is likely that the NCBI will enable patients to have access to these new and emerging therapies.

Conclusion

On behalf of our patients, we urge Congress to reauthorize both the NCBI and the C.W. Bill Young Cell Transplantation Program by approving the TRANSPLANT Act. We look forward to working with you and key stakeholders of the cord blood banking community—patients, physicians, transplanters, cellular therapists, researchers and cord blood banks—to ensure that this important bill is signed into law this year.

Chairwoman Eshoo, Ranking Member Burgess, and members of the Subcommittee, thank you for the opportunity to share my support for the reauthorization of the Stem Cell Therapeutic and Research Act.