

Transplantation and Cellular Therapy





## Reflections Profile of a Pioneer: Eliane Gluckman

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Eliane Gluckman is a hematopoietic stem transplant pioneer who had the courage and insight to perform the first umbilical cord blood transplant in 1988 in a child with Fanconi Anemia (FA). At the time, in vitro assays suggested that cord cells were enriched for hematopoietic stem and progenitor cells, but there were no traditional preclinical or animal studies to support this hypothesis. Eliane recognized the importance of performing the 'first in man' experiment, putting the appropriate safeguards in place and forging ahead. The transplant was successful and over the next four decades she expanded knowledge in the field. In 1995 she created a registry to capture outcomes of cord transplants in Europe (Eurocord) and published on thousands of such transplants. In 2012 through the Monaco Scientific Center, she created Monacord, broadening her research to understand how to extend innovative treatments for sickle cell disease to individuals in Africa.

In 1987 as a junior attending in pediatric hematology/oncology at Duke, I was caring for a young child with FA and marrow failure who lived in a small town in North Carolina. At that time, we used androgen therapy and transfusion to buy time. In reality, the only chance for long-term survival would be a marrow transplant, but the boy didn't have a matched related donor, which was the only donor option in those days. As the boy's condition worsened an opportunity arose. His mother became pregnant again, so we arranged for an amnio sample to be sent to Arleen Auerbach at the Rockefeller Institute (who had created the first registry of FA) to test for genetic mutations of the disease. She informed us that not only was fetus unaffected, it was HLA-identical to her brother,

Matthew Farrow. Arleen also informed us that several scientists at Memorial Sloan Kettering Cancer Center, led by Hal Broxmeyer and Ted Boyce, had created a company called Biocyte which was about to test whether cord blood could substitute for bone marrow as a source of stem cells for transplant. Dr. Broxmeyer had shown a few years earlier that cord blood was enriched for hematopoietic stem and progenitor cells and appeared to be more potent than bone marrow cells in serial transplantation and repopulating studies in mice. Hal had also worked out methods to cryopreserve and thaw (or "defrost", as he liked to say) cord cells preserving their viability enabling long term storage. At the same time, Dr. Pablo Rubinstein, an immunologist at the New York Blood Center, was working out methods to collect, anti-coagulate, cryopreserve, and bank cord blood for unrelated transplantation.

We met with Hal, Ted, Arleen, Matthew and his mother Judy at Duke to discuss whether the family would allow collection of their daughter's cord blood when she was born and use those cells to transplant their son. All agreed and Hal and his team arranged for Gordon Douglas, an obstetrician from NYU to attend the delivery of the baby in Salisbury, NC. After collection, Hal arranged transport of the cord blood to his lab in New York where it was cryopreserved and stored under liquid nitrogen until the transplant.

An essential next step was to identify a physician to conduct the cord blood transplant. The obvious choice was Dr. Eliane Gluckman, who had trained with Jean Bernard, Jean Dausset, Rainer Storb and Don Thomas, and developed the first successful conditioning regimen for marrow transplant of

https://doi.org/10.1016/j.jtct.2024.12.012

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**Figure 1.** Hal Broxmeyer at Indiana University with containers used to ship cord blood for transplant of Matt Farrow.

patients with FA. Because of a DNA repair defect, FA patients are unable to tolerate traditional doses of chemotherapy or irradiation. In retrospect, Eliane invented the first successful reduced intensity preparative regimen for hematopoietic transplantation. Today we know that reduced intensity regimens are successful in adults with hematological malignancies and children with congenital immunodeficiency syndromes and other conditions.

I called Eliane and asked her if she would be willing to meet with Hal and his team to talk about performing the transplant. She agreed to meet and ultimately perform the transplant. A few months later, the baby was born, the cord blood was collected, and shipped to Hal's lab where it was cryopreserved (figure 1). When the baby was 6 months old, an age when she could also serve as a bone marrow donor if the cord blood transplant failed to engraft, the family flew to Paris where they lived for the next 6 months. Eliane cared for Matthew, now 5 years old, in her transplant unit at Hospital Saint-Louis. Hal transported the cord blood to Paris in a dry shipper which 'sat' next to him on the plane. The cord blood was thawed at the bedside and infused after reduced conditioning preparation. Engraftment occurred at day 19 and the patient recovered uneventfully. He is alive today 37 years later, durably engrafted with his baby sister's cord blood (figures 2 and 3).

After this success, Eliane performed additional transplants in Paris and recognized that cord blood had unique properties, including immune tolerance and that cord transplants resulted in less graft-versus-host disease when compared to matched marrow grafts. She joined an international movement to bank unrelated cord blood and to use it as a partially matched donor source for individuals lacking matches in the family or unrelated donor registries. She recognized that cord blood donors met a medical need especially for patients of minority ancestry. Creation of the Eurocord Registry enabled Eliane to collect outcomes data for all cord transplants performed in the European Union. With the team she built at Eurocord, she analyzed large datasets and reported novel observations about the impact of cell dose and HLA matching on outcomes of cord blood transplants and collaborated with the CIBMTR in the United States. She became president of the European



**Figure 2.** Left, Matt Farrow, First Cord Blood Transplant Recipient for Fanconi Anemia and Eliane Gluckman, L'Hospital St Louis, Paris, 1988. Right, Alive and well 36 years later Matt is shown with Joanne Kurtzberg. Since 1989, over 50,000 umbilical cord blood units have been shipped for unrelated donor stem cell transplants for malignant and nonmalignant disorderes.

**Figure 3.** Left to right: Eliane Gluckman, Matthew Farrow, Hal Broxmeyer, and Joanne Kurtzberg in September 2019 upon presentation of the Cord Blood Association's Lifetime Achievement Award to Dr. Broxmeyer.

School of Haematology, the World Marrow Donor Association, was a founding member of EBMT and leader of women in science at a time of male predominance in hematology and other disciplines.

Over her career, Dr. Gluckman has received many prestigious awards. In 2010 she received the honorary prize of the French National Institute of Health and Medical Research (INSERM) and in 2017 was awarded the Grand Officer of the National Order of Merit for contributions to the French nation. As president of the Cord Blood Association, I was honored to give her it's first lifetime achievement award in 2018. Figure 3 depicts Hall Broxmeyer receiving the 2019 award. In 2022 she received the Lifetime Achievement Award from the Pediatric Transplantation and Cellular Therapy Consortium. In December 2024 she was awarded the William Coulter Lifetime Achievement Award from the American Society of Hematology which will be awarded at the annual meeting in San Diego in December 2024. A young investigator award named for her will be awarded at the European Bone Marrow Transplant meeting in Florence in April 2025.

Eliane is personable and charming who is at home on scientific and social stages. She can give the keynote address in an international meeting or entertain dinner guests late into the night. She once told me that she makes gefilte fish from herring by scratch in her bathtub. She has mentored hundreds of trainees, run training courses, and organized several international congresses focusing on cord blood biology and transplantation. Although she retired from practice more than a decade ago, she divides her time between Paris and Monaco, attending meetings and writing papers. She has often been called the mother of cord blood transplantation, a well-deserved title for this pioneer.

## AUTHOR PROFILE AND CONTRIBUTIONS TO THE FIELD

Joanne Kurtzberg is the Jerome Harris Distinguished Professor of Pediatrics, Professor of Pathology, and the founder and former Director of the Pediatric Blood and Marrow Transplant Program (now Pediatric Transplant and Cellular Therapy Program) at the Duke University School of Medicine. She is the Director of the Marcus Center for Cellular Cures (MC3) and is the Co-Director of the Clinical Stem Cell Transplant Laboratory of Duke Hospital. She founded and directs the Carolinas Cord Blood Bank - an FDA licensed public cord blood bank and member of the National Cord Blood Inventory. In 1993 she performed the first unrelated donor cord blood transplant in the world at Duke and pioneered the use of cord blood transplantation to treat babies and children with selected leukodystrophies. Her current research focuses on cord blood banking and transplantation and development of novel cell and gene therapeutics and therapies derived from cord blood and birthing tissues. She is a strong advocate for newborn screening for inherited leukodystrophies such as Krabbe Disease. She is the founder and President of the Cord Blood Association, member of the board of the Cord Blood Association Foundation, and leader of the standards committees for the FACT Netcord Standards for Cord blood Banking. In 2012 she was awarded a Lifetime Achievement Award from the Pediatric Blood and Marrow Transplant Consortium.