IMPACT REPORT: FRANCES AND THOMAS GAMBINO PROFESSOR OF HEMATOLOGY/ ONCOLOGY

Prepared for the Gambino Medical & Science Foundation

In collaboration with Jeffrey M. Lipton, MD, PhD

Chief, Hematology/Oncology and Stem Cell Transplantation
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Feinstein Institutes for Medical Research

January 1, 2025-December 31, 2025

Northwell Health®

THANK YOU

"The flexibility provided by philanthropic funding has been a powerful advantage for us, and I'm deeply grateful for your support. It allows us to pursue high-risk, high-reward ideas that traditional funding sources often won't support. I'm very excited about this work, and there's a real sense of discovery every time we step into the lab."

— Jeffrey M. Lipton, MD, PhD
Frances and Thomas Gambino Professor of Hematology/Oncology
Donald and Barbara Zucker School of Medicine at Hofstra/Northwell

Overview

Jeffrey M. Lipton, MD, PhD, and his colleagues are making important strides in understanding a rare blood disorder called Diamond-Blackfan anemia syndrome (DBAS),a rare inherited bone marrow failure syndrome that presents early in life and carries an elevated risk of cancer.

Research Highlights

Working closely with Northwell's Lionel Blanc, PhD, the Les Nelkin Professor of Pediatric Oncology, Dr. Lipton's laboratory has developed mouse models carrying mutations in ribosomal protein genes—specifically L5 and S19—that are known to cause DBAS in patients. These models are especially important because DBA is a disorder of the ribosome—the cell's protein-making machinery—and defects in ribosomal proteins disrupt normal blood cell development and increase cancer risk.

The first paper describing the RPL5 and RPSS19 mouse models was recently accepted in *Nature Communications* and demonstrates that these mice successfully reproduce key features of DBA. Rather than simply causing general illness, the mutations lead to specific, tissue-dependent problems, including defects in blood formation and the development of cancers such as leukemia and sarcoma. This represents a critical "proof of principle," enabling scientists to reliably recreate DBA in animals and study how it unfolds over time.

Importantly, the study also shows that where the mutation is turned on in the body matters. By directing the mutation to specific tissues, such as bone or blood-forming cells, the researchers can trigger different disease outcomes. This level of precision allows them to ask highly targeted questions about how cancer begins and progresses in DBAS.

Building on this work, the team has developed a bone-specific version of the S19 model and expanding its cancer-focused studies. These mice will allow researchers not only to understand disease mechanisms but also to test strategies for early detection, prevention and treatment of cancer in DBAS.

At the same time, Dr. Lipton's group is currently finalizing a large international study of approximately 2,500 patients. This work confirms a surprising finding: mutations in the gene RPS26—despite being linked to anemia and birth defects—may actually protect some patients from developing cancer. Understanding why this happens could open the door to entirely new therapeutic approaches. A mouse model is being developed to study this observation.

Global Collaboration and Recognition

Dr. Lipton's work includes building a highly collaborative international network of clinicians and scientists studying DBAS. This consortium has assembled one of the largest patient registries in the world, enabling researchers to validate findings across different populations and healthcare systems.

These collaborations are essential for rare diseases like DBAS, where no single country has enough patients to fully understand the condition. By combining data globally, the team can

identify meaningful patterns, such as cancer risk and genetic differences, that would otherwise remain hidden.

The group will convene at the European Global Bridges Conference on Diamond-Blackfan anemia syndrome in Toulouse, France, where researchers will share findings, refine strategies and bring new investigators into the field.

Strategic Priorities

Looking ahead, Dr. Lipton and his colleagues are focused on translating these discoveries into real-world impact. One key priority is expanding mouse models to study colorectal cancer, an emerging concern in DBAS patients, particularly at younger ages. Collaborations with researchers at Cold Spring Harbor Laboratory will help the team adapt existing colon cancer models and apply their tissue-specific mutation approach.

Another major goal is to better understand why certain genetic mutations, like RPS26, appear protective against cancer. If researchers can uncover the biological mechanism behind this effect, it could lead to new therapies that mimic this natural protection.

Finally, the team is working to develop clearer screening and surveillance strategies for patients. While cancers such as breast, colon cancer and skin cancer can be monitored relatively easily, others—like bone cancer pose greater challenges, especially in young individuals.

NORTHWELL HEALTH ENDOWMENT PERFORMANCE

January 1, 2025 – December 31, 2025

Endowment overview and spending policy

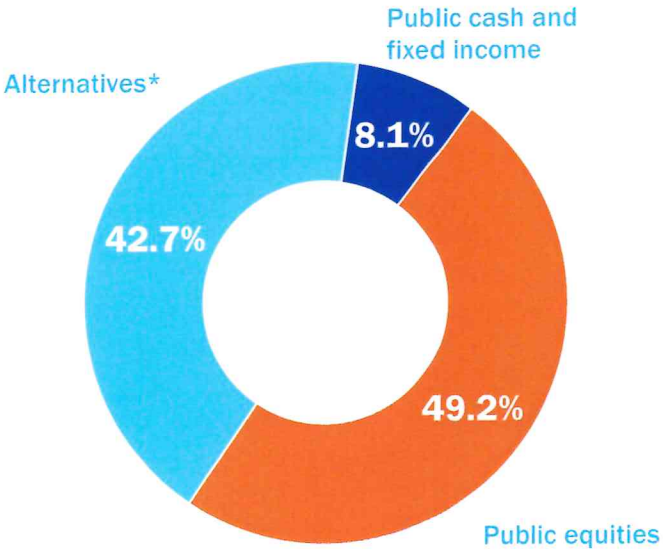
Northwell Health endowments are overseen by the Investment Subcommittee of the Finance Committee of the Board of Trustees, in conjunction with the organization's treasury department and investment consultants. The Investment Subcommittee regularly reviews the asset allocation of the endowment portfolios in relation to diversification and spending objectives and tracks the performance of each investment manager against an appropriate benchmark index.

The endowment portfolios are invested with a long-term growth objective and meet the expense and income needs of the projects they support. The goal of the portfolio design is to build a diversified set of investment strategies to generate good returns while minimizing risk and volatility over the portfolio's time horizon.

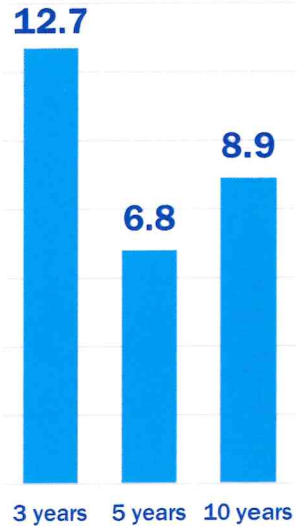
The spendable interest credited annually to all endowment funds is based upon a rolling average of the return on the Northwell Health Endowment Portfolio over the prior five years, calculated annually on or about June 30 of each calendar year, and will not exceed 5%. For the calendar year ending December 31, 2025, the spendable interest credited to all endowment funds was 5%.

ASSET ALLOCATION

As of Dec. 31, 2025



HISTORIC ENDOWMENT PERFORMANCE



*Alternatives

- 16.5% hedge
- 24.5% private equity/real estate
- 1.8% private credit

ACCOUNT ACTIVITY

Corpus — $2,740,920

The amount that has been donated to the endowment is permanently restricted and required to be held in perpetuity.

Market Value — $3,023,414

The value of the investments that support this endowment on the date specified. This figure indicates both the corpus and earnings, but not the spendable interest, and fluctuates with the financial markets.

Spendable Interest Earned for Reporting Period — $81,360

Interest that can be spent on the endowed purpose. Begins to accrue at the start of the calendar year after endowment reaches minimum gift amount.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