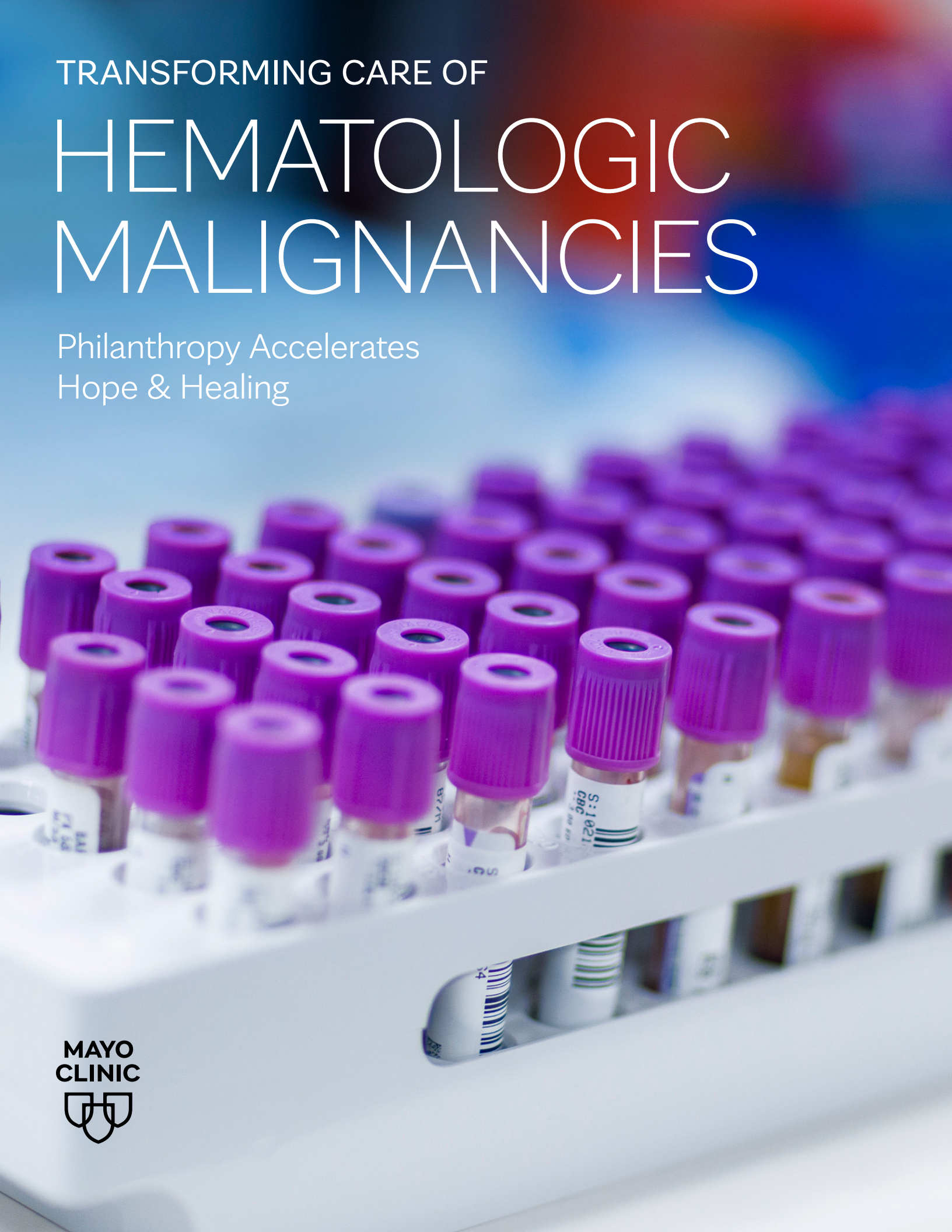
TRANSFORMING CARE OF

HEMATOLOGIC MALIGNANCIES

Philanthropy Accelerates Hope & Healing



MAYO CLINIC

Contents

MAYO CLINIC IS DEDICATED TO TRANSFORMING OUTCOMES AND **ENHANCING THE QUALITY OF LIFE FOR PATIENTS LIVING WITH HEMATOLOGIC MALIGNANCIES,** FROM THE MOST COMMON TO THE RAREST FORMS.

Mayo Clinic has long been at the forefront of advancing hematologic malignancies care. With specialty bone marrow transplant care, novel cancer-targeting therapeutics, advanced diagnostics that detect single cancer cells among millions, extensive biobanks tracking long-term outcomes, pioneering staging and classification systems, and the first molecular tests that assess gene mutation impacts on prognosis, Mayo physicians and scientists are internationally recognized for their expertise in this field.

On behalf of patients, we strive to do more. Our research teams continue to develop the next generation of cures, including bioengineered cellular therapeutics in facilities at Mayo Clinic to help the immune system recognize and destroy cancer. Mayo is also expanding access to care for patients in their local communities and making therapies widely available to improve lasting remission for survivors.

Underpinning these efforts is an intentional approach to integrating artificial intelligence (AI) within research and patient care to enhance diagnostics, develop novel therapeutics and personalize treatments. Leveraging Mayo's expansive datasets, researchers are rapidly translating scientific discoveries — performing complex analyses to characterize tumors, define underlying biology, find genetic markers that influence cancer cell behavior, and identify factors linked to treatment resistance and relapse.

Mayo Clinic is pursuing innovative science that is **reshaping our understanding of hematologic malignancies** and setting new global standards of care.

GENEROUS SUPPORT FROM OUR BENEFACTORS MAKES THIS POSSIBLE.

123

clinical trials in hematologic malignancies (not all open to enrollment) in 2024

LYMPHOID MALIGNANCIES

Mayo Clinic experts diagnose and treat all subtypes of lymphoma and chronic lymphocytic leukemia (CLL).

Mayo Clinic is renowned in innovating care for these blood cancers. Our scientists and physicians have pioneered advancements for patients, including establishing the diagnostic criteria for the precursor stage of chronic lymphocytic leukemia and investigating therapeutics for Hodgkin and non-Hodgkin lymphomas.

Lymphoma

Chronic Lymphocytic Leukemia

BENEFACTORS FUEL THESE ADVANCES THROUGH THEIR **GENEROUS SUPPORT.**

14,600+

patients treated at Mayo Clinic in 2024 (CLL and lymphoma combined)

Lymphoma

HOPE FOR YOUNGER PATIENTS **WITH LYMPHOMA**

Brescia's story

Mayo Clinic's Adolescent and Young Adult Cancer Program helps patients navigate the complexities of care and serves their unique needs as they undergo physical, emotional and social development while in treatment. Brescia Dover was 20 when she was diagnosed with Hodgkin lymphoma. "Being diagnosed with cancer at 20 years old was so scary, and I wouldn't wish that on any 20-year-old," she says. Brescia received chemotherapy at Mayo Clinic, where clinicians balance the risk of relapse and the risk of lasting side effects for their younger patients. Mayo's investigators continue to study specific issues that affect this age group, including the impact on fertility and the toxicities of novel therapeutic treatments.

Following her treatment, Brescia graduated from college and started a marketing agency. **She recently celebrated five years of being cancer-free.**

Non-Hodgkin Lymphoma

FINDING CURES FOR **RELAPSED NON-HODGKIN LYMPHOMA**

Mayo Clinic investigators are advancing targeted treatment strategies in diffuse large B-cell lymphoma (DLBCL) with new insights about relapse mechanisms. DLBCL is the most common adult non-Hodgkin lymphoma in the U.S. In up to 40% of cases, the disease does not respond to treatment, leading to tumor progression. Mayo's research first identified mutations in the SPEN gene in patients with DLBCL who had tumor progression within two years after treatment. The research team then performed multi-omics analysis, studying biological molecules and processes in cells and tissues, on newly generated laboratory models from DLBCL tumors collected over two decades at Mayo. They completed an extensive characterization of tumors with various mutations to define the active mechanisms in aggressive tumors. The resulting data is critical to anticipating early progression and developing novel approaches for relapsed disease.

AI AIDING **CHRONIC LYMPHOCYTIC LEUKEMIA** CARE

Mayo Clinic recently advanced diagnostic capabilities in chronic lymphocytic leukemia (CLL) with the development of generative AI models, trained on Mayo's vast datasets to identify the presence of minimal residual disease after treatment. The models help with repetitive tasks and subjective interpretation in complex analysis, leading to more efficient results.

Investigators are now building a pipeline for minimal residual disease analysis in other diseases. They are also scaling up AI models for an important cytogenetic test known as fluorescence in situ hybridization that looks for specific changes in genes or chromosomes in CLL cells and **helps clinicians plan treatments for patients.**

MYELOID MALIGNANCIES

Mayo Clinic hematologists, pathologists, radiation oncologists, radiologists and transplant specialists work as a multidisciplinary team across Mayo Clinic to care for patients with all subtypes of **acute leukemia and myeloid neoplasms.**

Acute Leukemia and Myeloid Neoplasms

Mayo Clinic has an unparalleled ability to build a unique and personalized treatment plan that meets the needs of each patient. Clinical and diagnostic excellence, the translation of scientific discoveries, platform-enabled clinical trials, and in-house world-class biomanufacturing capabilities make this possible.

OUR PARTNERSHIPS WITH GENEROUS BENEFACTORS ARE **HELPING USHER IN THIS REVOLUTION IN CANCER CARE.**

9,300+

patients treated at Mayo Clinic in 2024 (acute leukemia and myeloid neoplasms combined)

ESTIMATING THE INCIDENCE OF **ERDHEIM-CHESTER DISEASE IN THE UNITED STATES**

Erdheim-Chester disease (ECD) is a rare blood cancer that affects multiple organ systems, yet little is known about how often it occurs in the United States. ECD is difficult to diagnose due to its wide range of symptoms, which can affect bones, the brain, the heart and other organs. While targeted therapies and chemotherapy are available, the disease remains complex and underrecognized. In 2021, only 16 cases were reported. Using data from the National Cancer Institute's SEER program, we aim to establish the first accurate estimate of ECD's occurrence — a critical step toward understanding this rare disease, improving early detection, and ensuring patients receive timely and effective treatment.

Mayo Clinic laboratory technician

GENETIC APPROACHES TO **LEUKEMIA AND MYELOID NEOPLASMS**

Mayo Clinic hematologists are diagnosing and managing rare genetic syndromes that contribute to bone marrow failure. This is possible through a field-leading clinical and diagnostic clinic that first opened at Mayo's campus in Rochester, Minnesota, and soon will open at campuses in Florida and Arizona. In an interventional clinical trial as part of the bone marrow failure clinic, investigators are testing next generation sequencing — new technology that looks at cancer-associated genes. Their novel diagnostic platform identifies patients who may be at risk of developing leukemia and myeloid neoplasms through the detection of genetic mutations. It identifies the risk for precursor conditions and the likelihood these will progress to cancer.

Leukemia

PREDICTIVE TOOL **FOR LEUKEMIA**

Researchers at Mayo Clinic and partner institutions discovered that cumulative chromosomal changes in plasma cell leukemia, a rare type of multiple myeloma, can make the disease more aggressive and difficult to treat. Plasma cell leukemia involves high numbers of cancerous plasma cells in the bloodstream, unlike typical multiple myeloma. The study compared outcomes over a decade in cases involving multiple or single high-risk cytogenetic abnormalities. These abnormalities affect the structure or number of chromosomes, leading to faster cancer growth and resistance to treatment. Patients with multiple high-risk cytogenetic abnormalities had shorter survival times compared to those with only one.

This work offers clinicians a key prognostic tool for **personalized treatment plans.**

MYELOMA

Multiple myeloma is a relatively uncommon form of blood cancer that forms in a plasma cell. Healthy plasma cells help the body fight infections by making antibodies that recognize and attack germs.

Multiple Myeloma

In multiple myeloma, cancerous plasma cells accumulate in the bone marrow and crowd out healthy blood cells. Rather than produce helpful antibodies, the cancer cells produce abnormal proteins that can cause complications. While there is no cure, the disease can be treated with medication, chemotherapy, radiation and even bone marrow transplant.

Mayo Clinic doctors and scientists have been at the forefront of multiple myeloma research for more than 50 years and have contributed important findings to the understanding of this cancer. This includes the Mayo Clinic Multiple Myeloma Specialized Program of Research Excellence from the National Cancer Institute to speed translation of the most promising science to the clinic.

OUR WORK IS POSSIBLE BECAUSE OF THE **GENEROUS SUPPORT OF BENEFACTORS.**

4,600

patients treated at Mayo Clinic in 2024 (myeloma)

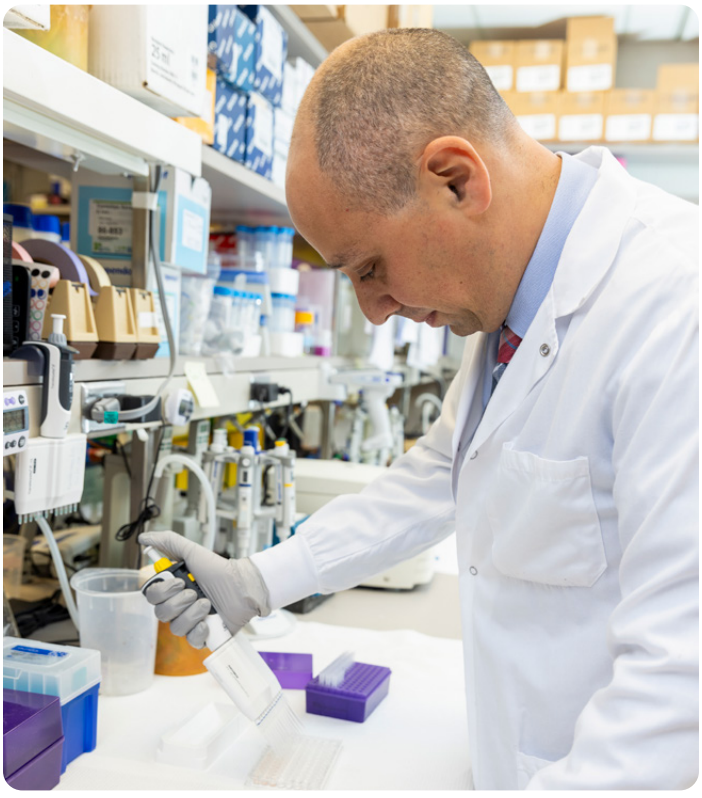
ADVANCING MULTIPLE MYELOMA TREATMENT THROUGH NOVEL MOLECULAR TARGET AND PREDICTIVE BIOMARKER DISCOVERY

Mayo Clinic researchers are investigating new ways to improve treatment for multiple myeloma, an incurable blood cancer. A new study aims to identify protein markers that indicate disease aggressiveness, unique cancer cell features that could enhance immune system recognition, and new drug targets for treatment-resistant cases. Through extensive analysis of patient samples and cell lines, researchers have uncovered thousands of unique protein markers, including previously unknown ones.

These findings could lead to **more precise diagnostic tests, improved immunotherapies and novel drug options.**

DUAL-TARGET CAR-T THERAPY AND 'IMMUNOMETER,' AN INNOVATIVE MONITORING TOOL

Multiple myeloma remains incurable partly because cancer cells hide within a protective environment. Researchers are developing a novel CAR-T therapy that targets both cancer cells and tumor-associated macrophages (TAMs), which help the disease resist treatment. This dual-targeting approach may improve effectiveness and reduce relapse. To enhance safety and accessibility, we developed the "Immunometer," a simple blood test that tracks CAR-T cell activity using a drop of blood. This tool offers a faster, less invasive way to monitor treatment responses. By attacking both cancer cells and their support system while simplifying patient monitoring, we are making CAR-T therapy more effective and widely available.



ON THE HORIZON

AI MODELS ADVANCE **LYMPHOMA TREATMENT**

Mayo Clinic investigators are leveraging vision-language foundation models, a type of AI that simultaneously learns from images and text, such as medical scans and patient reports, for personalized care. The first initiative is called Lymphovision, in collaboration with Mayo Clinic's team from the Lymphoma Specialized Program of Research Excellence. The model is working with more than two decades of data gathered from diverse national cohorts to improve diagnostics and forecast how a patient might respond to therapy in lymphoma. The second initiative is called Blood Bytes. The foundation model will examine single-cell images from blood and bone marrow for more comprehensive characterization of cellular biology to identify targets and develop predictive biomarkers for response to novel therapies.

UNDERSTANDING INHERITED RISK FACTORS OF CLL

TO IMPROVE EARLY DETECTION AND THERAPIES

While advances in treatment have improved outcomes, CLL remains incurable and increases the risk of infections and secondary cancers. Despite evidence that inherited genetic factors contribute to CLL, the underlying mechanisms remain unclear. Through benefactor support, scientists are analyzing key genetic markers that influence leukemia cell behavior and survival. Using cutting-edge genetic tools, they are mapping how specific genetic sites contribute to disease progression. This work is reshaping our understanding of CLL. By identifying these inherited risk factors, we will uncover critical pathways for early detection and precision therapies.

OPTIMIZING STEM CELL TRANSPLANT SUCCESS

Allogeneic stem cell transplantation is a lifesaving treatment for blood cancers, but complications like graft-versus-host disease and transplant failure remain challenges. Researchers at Mayo Clinic are exploring how different pre-transplant conditioning therapies impact the bone marrow environment and recovery. Early findings show that while intensive chemotherapy and radiation support donor cell engraftment, they may also slow overall recovery. Less intensive regimens appear to better preserve bone marrow structure, potentially aiding long-term healing.

By identifying the best strategies to balance engraftment and recovery, we aim to improve transplant success, reduce complications and long-term morbidity, and **enhance survival rates for patients while making this curative therapy safely available for more patients with high-risk leukemia and myeloid neoplasm.**

MULTI-OMICS OF HIGH-RISK
MULTIPLE MYELOMA

Extensive studies confirm that genetic disruptions play a key role in multiple myeloma. Its evolution, before and during therapy, results from complex interactions between genetic changes and environmental factors. Yet, for unknown reasons, effective therapies fail in the highest-risk patients. To address this, we are launching the first longitudinal clinical trial and data resource to map gene-environment interactions in high-risk cases. Using a well-studied, homogeneously treated group, we will analyze genomic, immune, and metabolic changes at the highest resolution to uncover pathways affecting treatment response.

EARLY DETECTION AND PREVENTION
OF MULTIPLE MYELOMA PROGRESSION

Multiple myeloma is preceded by a common benign monoclonal plasma cell expansion called monoclonal gammopathy of undetermined significance (MGUS). In between multiple myeloma and MGUS is a third clinical entity called smoldering multiple myeloma. In this condition, there is more-extensive plasma cell expansion than in MGUS, but the malignant features of multiple myeloma are not seen. This study aims to define the genetic events that drive multiple myeloma progression from a benign state to a malignant state. By using next-generation sequencing, researchers analyze genetic mutations and pathways linked to disease advancement. They also study how the tumor microenvironment contributes to progression. The goal is to create a genetic definition of malignant plasma cells, enabling earlier detection and intervention, ultimately transforming how the disease is diagnosed and treated.

Philanthropic support empowers Mayo Clinic hematologic malignancies researchers and physicians, impacting people around the globe.

ON BEHALF OF OUR PATIENTS AND STAFF EVERYWHERE, **THANK YOU.**

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