MAYO CLINIC

# Desert Mountain CARE

**Stewardship Update | June 2026**

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# Philanthropy accelerates hope and healing

The long-standing partnership with Desert Mountain CARE and its members continues to propel Mayo Clinic in Arizona's bold vision for the future of cancer care. Through your generosity, investigators are exploring innovative approaches to better understand and treat some of the most complex and difficult cancers, bringing new possibilities to patients and families.

We are honored to share the enclosed updates, highlighting the progress made possible through your generosity. In the following pages, investigators describe how their work is expanding knowledge of cancer biology and advancing more precise, personalized approaches to care.

With sincere appreciation, we recognize the far-reaching impact of your philanthropy. Your investment fosters discovery, strengthens collaboration and builds momentum — ensuring that promising ideas move forward and translate into meaningful improvements for patients today and in the years ahead.

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**Fonti Gounari, Ph.D.**
Professor of Immunology

## PROJECT 1: PATHOGENESIS OF MYC-OVEREXPRESSING ACUTE LEUKEMIA

Acute lymphoblastic leukemia (ALL) is the most common cancer in children and remains a leading cause of cancer-related death in young people. This research focuses on understanding how a cancer-causing gene called MYC becomes abnormally activated in leukemia cells. MYC functions as a master regulator of cell growth. When overactivated, it can drive the transformation of normal blood cells into aggressive cancer cells.

This project aims to define the molecular events that lead to MYC activation and leukemia development. Using a unique mouse model that closely mimics genetic alterations seen in a subset of patients with T-cell ALL, researchers examined how changes in the DNA regions controlling MYC expression contribute to cancer. By identifying the factors that switch MYC on and sustain its activity, this work seeks to uncover new opportunities for earlier detection and more effective therapies.

## RESEARCH UPDATES

A major accomplishment of this project has been the discovery of a previously unknown mechanism driving MYC-dependent leukemia. Researchers identified a protein called TCF-1, normally essential for healthy immune cell development, as a key requirement for leukemia formation in this model. When TCF-1 is removed, leukemia does not develop, revealing its central role in cancer transformation. This finding offers an entirely new perspective on how MYC becomes activated and opens promising avenues for therapeutic development.

In addition, investigators identified significant changes in the structure and organization of DNA surrounding the MYC gene. These alterations create an abnormal “super-enhancer,” a powerful regulatory element that drives continuous, high levels of MYC expression. Studying these processes is technically complex, as they involve three-dimensional interactions within the genome. Despite these challenges, the research group successfully generated the genomic and molecular datasets needed to uncover these mechanisms. These findings now support a new National Institutes of Health (NIH) grant application and a manuscript currently in preparation.

## PATIENT IMPACT

While this work remains at the laboratory stage, it addresses a fundamental question in leukemia biology: Why do some cells become cancerous while others remain healthy? Understanding these earliest events is essential to developing better strategies to prevent, detect and treat leukemia.

These findings suggest that processes controlling MYC activation, including TCF-1 and the surrounding regulatory DNA, may represent future therapeutic targets. Rather than broadly attacking cancer cells, future therapies could potentially disrupt the specific mechanisms leukemia cells rely on to grow and survive. This more precise approach has the potential to improve outcomes while reducing treatment-related side effects for patients.

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## LOOKING AHEAD

A central discovery from this work is TCF-1's dual role: it supports normal immune cell development while also promoting cancer initiation as shown in **Figure 1.**

The team found that TCF-1 is helping activate a cancer-promoting MYC super-enhancer by reaching a critical regulatory region near MYC and helping create the molecular conditions leukemia needs to develop. This unexpected finding reveals a new layer of control over cancer-causing gene activation, illustrated in **Figure 2**.

Next, researchers will define how TCF-1 activates this regulatory region and whether leukemia continues to depend on it after the disease is established. They are also studying enhancer RNAs, a newly identified class of molecules that may help sustain MYC activity. Together, these efforts could reveal vulnerabilities for future targeted therapies.

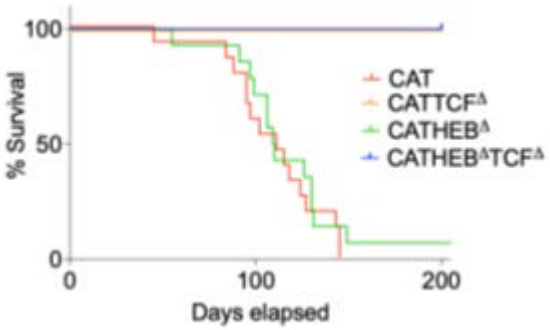


**Figure 1.** Survival analyses show that leukemia does not develop when TCF-1 is removed (CATHEBDTCFD), demonstrating TCF-1 is essential for leukemia formation.

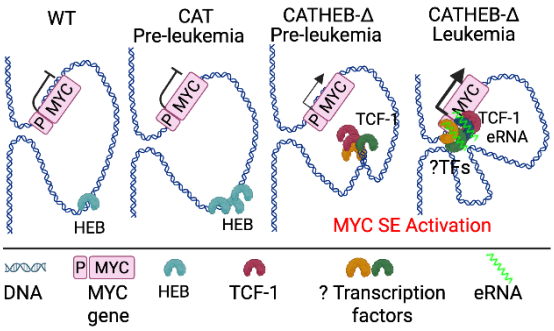


**Figure 2:** Proposed super-enhancer activation steps based on genetic mutation and leukemia state.

## IMPACT OF PHILANTHROPY

The generous support of Desert Mountain CARE has been instrumental in advancing this research. Philanthropic funding allowed us to pursue innovative ideas that would have been difficult to explore through traditional funding mechanisms alone, enabling the generation of critical preliminary data, development of specialized experimental models, and collection of the genomic datasets that led directly to these discoveries.

Most importantly, this investment helped uncover a new mechanism of leukemia development and provided the foundation for a competitive NIH grant application that will allow us to continue expanding this work. On behalf of our entire research team, I would like to express our sincere gratitude for your partnership and vision. Your support is accelerating discoveries that bring us closer to more precise and effective treatments for patients and families affected by leukemia.

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**Felipe Batalini, M.D.**
Assistant Professor
of Medicine

# PROJECT 2: FAST NEOEPITOPE PRIORITIZATION AND RNA NANOPARTICLE DENDRITIC CELL VACCINES FOR SOLID TUMORS

This project focuses on advancing personalized treatment strategies for women with BRCA-related breast cancer by studying how tumors respond to therapy at both the genomic and immune levels. The research centers on identifying biomarkers that help explain why some patients respond to treatment while others do not, particularly among tumors with homologous recombination deficiency.

A key area of this work involves studying neoepitopes, which are unique markers created by genetic changes in cancer cells. These markers have the potential to help the immune system recognize and target tumors more effectively. To support this effort, the team is developing and validating advanced computational tools to predict neoepitopes, alongside laboratory studies to confirm their ability to trigger immune responses. Ultimately, this research aims to lay the foundation for a novel immunotherapy approach targeting these tumor-specific markers.

## RESEARCH UPDATES

Over the past year, the team has made significant progress in processing and analyzing breast cancer samples. To date, 18 biobanked tumor samples have been collected, with 12 successfully sequenced using advanced long-read sequencing techniques. Additional RNA sequencing was performed to validate these findings, ensuring accuracy before advancing to further immunologic analyses.

Through iterative refinement of sample processing and sequencing methods, the team achieved reliable quality control and established a robust workflow. These efforts led to the development of a computational pipeline capable of identifying neoepitopes derived from gene fusions as well as single nucleotide variants. Importantly, the team demonstrated that neoepitopes can be effectively identified from frozen tumor samples, while also determining that certain preserved tissue types are not suitable for this approach — an insight that has helped refine ongoing protocols and improve efficiency.

As with many pioneering studies, the project encountered challenges, including limited access to high-quality tissue samples and the cost associated with repeated technical testing. However, these obstacles prompted important refinements in both sample collection and analytical methods, ultimately strengthening the overall study design.

## PATIENT IMPACT

Breast cancer remains one of the most common cancers affecting women worldwide. While major advances have improved outcomes, many patients, including those with inherited BRCA1 and BRCA2 mutations, continue to face difficult treatment decisions and the risk of disease recurrence. This project aims to develop a new generation of personalized immunotherapies that leverage each patient's unique tumor biology to stimulate an immune response against cancer.

Over the past year, support from this award enabled the development of the laboratory and computational methods necessary to identify patient-specific cancer neoepitopes using long-read sequencing technologies. These advances represent an important step toward creating individualized immunotherapies that we plan to evaluate in a clinical trial, pending Food and Drug Administration authorization. This provides hope for more precise and effective treatment options for patients with breast cancer and other solid tumors.

## LOOKING AHEAD

The team has built a strong foundation for continued progress, including a computational pipeline that can rapidly identify neoepitopes from multiple types of genetic alterations. Researchers also improved workflows for tissue collection, preservation and processing, helping ensure higher-quality samples and more reliable results.

The next phase will focus on validating the most promising neoepitopes in the laboratory and advancing a personalized immunotherapy strategy. This approach uses mRNA-based dendritic cell therapies designed to train the immune system to recognize and attack cancer cells.

Over the next 1 to 2 years, investigators plan to pursue regulatory approval and launch a phase 1 clinical trial at Mayo Clinic. Ongoing collaborations with clinical, surgical and industry partners are helping position this work for successful translation into patient care.

## IMPACT OF PHILANTHROPY

On behalf of our research team and the patients we serve, I would like to express my sincere gratitude to the Desert Mountain CARE Program and its members for supporting this work.

Philanthropic funding plays a unique role in advancing innovative, high-risk, high-reward science that is often difficult to support through traditional funding mechanisms. Your generosity has allowed us to establish critical laboratory and computational capabilities, evaluate new sequencing technologies, generate preliminary data, and advance the development of a personalized cancer immunotherapy platform.

Importantly, your investment has enabled exploration of new questions that may lead to entirely novel treatment approaches for patients with cancer. The progress achieved thus far, including the development of methods to identify actionable neoepitopes and the advancement of plans for clinical translation, would not have been possible without your partnership.

We are deeply grateful for your confidence in our work. Your support is helping move promising discoveries closer to patient application, with the potential to improve outcomes for individuals and families facing cancer.