BIOMARKERS CONSORTIUM

FNIH

# Defining Tumor and Immune Markers to Stratify Patients at Risk of Developing Multiple Myeloma from MGUS and Smoldering Myeloma

## PROJECT OBJECTIVE

This project will evaluate tumor and immune biomarkers to predict progression from early precursor conditions to multiple myeloma and identify patients likely to benefit from early therapeutic intervention.

## UNMET MEDICAL NEED

Multiple Myeloma (MM) is the second most common hematologic malignancy in the US and is almost always preceded by precancerous conditions including monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM). These conditions affect ~3% of people over 50 years old and are up to three times more likely to occur in African Americans and in people with a family history of MM. Annually, ~1% of MGUS cases progress into SMM, of which half will then progress to MM within 2 years.

Early therapeutic intervention at the SMM stage has shown improved progression-free survival (PFS) and prevention of morbidity from end-organ damage. Currently, the only ways to assess a patient's risk of progression from MGUS or SMM to MM require a bone marrow biopsy, which is invasive and presents risk to patients. These evaluations are also relatively simplistic, relying on manual estimates which are limited in accuracy and sensitivity. Consequently, most patients are not evaluated for risk and are not treated until they develop MM. There is an urgent need to accurately define the patient population at risk for developing MM and to intervene early to prevent end-organ damage and improve survival.

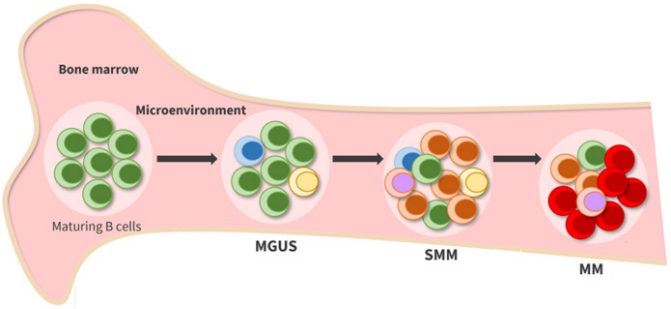
This project will use genetic sequencing of bone marrow and peripheral blood samples to develop prognostic biomarkers and monitoring tools for response to therapy in patients with MGUS and SMM. Using blood-based evaluations in lieu of painful bone marrow biopsies would reduce patient discomfort and disease monitoring cost. This less invasive method is also expected to increase utilization of early assessments of disease progression to generate opportunities for faster intervention, improved options for treatment, and hopefully, subsequent increase in patient response and survival.

## KEY AIMS

*Aim 1.* Develop a blood-based assessment of disease burden and tumor biology, as well as a prognostic biomarker for patients with MGUS/SMM.

*Aim 2.* Validate the blood-based biomarkers to be used for identifying the high-risk population that will develop myeloma.

**Stages of Progression to Multiple Myeloma**



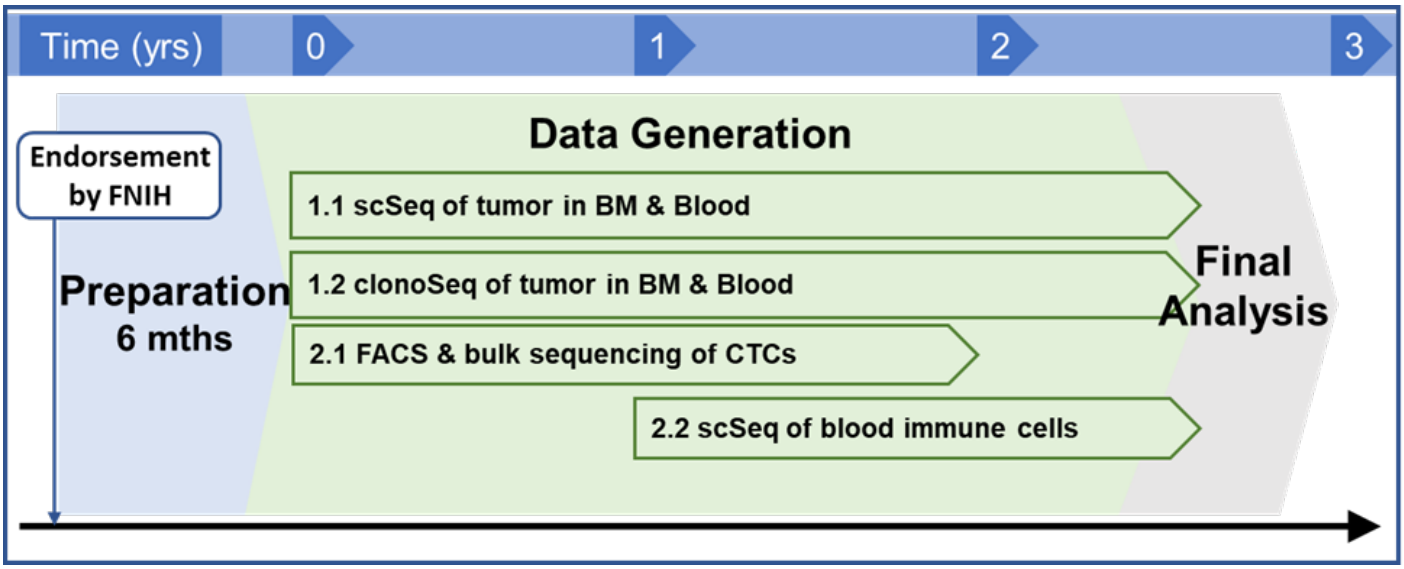

*Green circles represent healthy cells. Additional colors represent genetic changes associated with disease progression.*

*Credit: https://multiplemyelomahub.com/medical-information/precision-medicine-in-multiple-myeloma*

## PROJECT DELIVERABLES

- Development and validation of predictive tumor and immune biomarkers of progression from MGUS/ SMM to MM
- Bone marrow and blood-based immune profiling for prognostication of patients with MGUS/SMM and monitoring of response to treatment

## PROJECT TIMELINE




## OPPORTUNITIES FOR INVOLVEMENT

The FNIH actively seeks private-sector funding and budget-relieving in-kind resources to support this project. The project requires $6M in private funds over three years. The illustrative chart below outlines the contributions necessary for participation as a full-funding partner. The range of necessary financial contributions is ultimately dependent upon the number of participating funding partners.

| NUMBER OF PARTNERS | TOTAL COST PER PARTNER | ANNUAL COST PER PARTNER |
|---|---|---|
| 3 PARTNERS | $2,000,000 | $666,666 |
| 4 PARTNERS | $1,500,000 | $500,000 |
| 5 PARTNERS | $1,200,000 | $400,000 |
| 6 PARTNERS | $1,000,000 | $333,333 |

Full-funding partners may have multiple participants on the Project Team and may cast one vote per organization on project decisions. Throughout the life of the project, the FNIH will work to ensure that all partners have ample opportunity to provide input and share valuable expertise. Active participation and broad acknowledgment of all private partners will be facilitated through:

- Participation on the Project Team and in regular Project Team teleconferences
- Progress reports provided by the Project PIs and at least one face-to-face meeting per year
- Collaboration with FNIH staff to ensure recognition in press releases, project related print materials, the FNIH annual report, and the fnih.org website.

*To learn more about becoming a scientific and funding partner in the MGUS Project, please contact:*

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