YaleNewHaven**Health Smilow Cancer Hospital**

Grand Rounds

Tuesday, February 4, 12:00pm

Smilow Auditorium, 55 Park Street Join us in person for lunch Zoom Access

THE GENETICS OF MYELOID MALIGNANCIES: FROM GERMLINE **RISK TO SOMATIC TRANSFORMATION**

Coleman Lindsley, MD, PhD

Associate Professor of Medicine, Dana-Farber Cancer Institute, Harvard Medical School; Director, Edward P. Evans Center for MDS

Needs:

1.Clinical Gap in Genetic Risk Assessment for Leukemia: There is a need to address the gap in understanding and identifying germline mutations, such as TERT, that contribute to the progression of clonal hematopoiesis to AML. Many clinicians may lack the competence to effectively assess and stratify patient risk based on these genetic factors, which can impact treatment decisions and outcomes.

2.Need for Enhanced Clinical Surveillance Strategies: Current clinical practices may not fully integrate the latest insights from mechanistic pathways of leukemogenesis, particularly concerning patients with short telomere length. There is a need for education on developing and applying enhanced surveillance strategies to better manage and mitigate treatment-related toxicities

3.Advancements in Genomic Classifications and Treatment Planning: With recent advancements in genomic research, there is a need for clinicians to utilize updated genomic classifications, including mutations in histone epigenetic modifiers and RNA splicing, to inform treatment plans. This need is driven by the clinical gap in applying these classifications to improve patient outcomes in AML, especially in the context of bone marrow transplantation and novel therapies.

Objectives:

- 1. Understand the Genetic Drivers of Leukemia Progression 2. Utilize Genomic Classifications for Improved Outcomes
- 3. Analyze Genetic Risk Factors for leukemia development







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Dr. Coleman Lindsley is Associate Professor of Medicine at Harvard Medical School and Dana-Farber Cancer Institute. He received his MD and PhD in Immunology from Washington University School of Medicine, then completed a residency in internal medicine at Brigham and Women's Hospital and a fellowship in oncology at the Dana-Farber Cancer Institute.

He is a member of the MDS Genetics Subcommittee for the NIH National MDS Study, NHLBI **Trans-Omics for Precision** Medicine Steering Committee, and the International Working Group for Prognosis in MDS (IWG-PM) molecular committee.

The primary focus of his laboratory is the biology and treatment of myeloid malignancies. His genetic studies have led to new genomic models of leukemia classification and MDS outcome after stem cell transplantation. His laboratory uses mouse and cell line models to dissect the mechanistic basis of genetic cooperation during myeloid disease progression, with a specific focus on leukemia initiation in patients with predisposition syndromes and mutations that cause epigenetic alterations.



