Weill Cornell Medicine

Method for Biopsy-Free Enrichment and Analysis of Peripheral Blood Mononuclear Cells

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Background & Unmet Need

- Blood stem cells (HSPCs*) reside in bone marrow, give rise to blood cells, and underlie many hematologic diseases
- Diagnosis and prognosis of these diseases requires costly and invasive bone marrow biopsies
- HSPCs are also self-renewing precursors to immune cells, and varied immune response is implicated in inflammatory, autoimmune, and infectious diseases
- Studies in animal models show that HSPCs can maintain durable epigenetic memory of inflammation and pass it down to their progenitor immune cells
- The study of altered hematopoiesis and of innate immune memory in humans is challenging due to the invasive nature of acquiring samples of bone marrow, where these stem cells reside
- **Unmet Need:** non-invasive acquisition of blood stem cells for diagnosis, prognosis, biomarker and therapy development for inflammatory and hematologic diseases

Technology Overview

- **The Technology:** Methods for the enrichment and analysis of rare circulating HSPCs in blood samples
- **The Discovery:** While rare (0.05%), HSPCs do circulate in blood and accurately capture the diversity of stem cells that reside in the bone marrow
- PBMC-PIE** recapitulates bone marrow HSPC subsets, enables HSPC gene expression analysis, and reveals disease signatures of blood stem cells
- PBMC-PIE serves as a powerful tool to study hematopoiesis, epigenetic programming of HSPCs, and innate immune memory of inflammation without directly accessing the bone marrow
- **PoC Data:** Blood from 112 COVID-19 patients and 47 controls was analyzed using PBMC-PIE coupled with chromatin and expression analysis, enabling detailed single cell profiling of HSPCs and revealing increased myelopoiesis, neutrophil differentiation, and durable epigenetic signatures persisting in HSPCs up to a year post COVID-19

Inventors:
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Patents:
US Application Filed
PCT Application Filed
Provisional Filed

Publications:
Daman et al. *Cancer Cell*. 2025.
Cheung et al. *Cell*. 2023

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Cornell Reference:
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Technology Applications

- Non-invasive alternative to routine bone marrow biopsy for anemia, leukemia, lymphoma
- Diagnostic/prognostic assays, and drug target discovery for inflammatory, autoimmune, infectious diseases, post-viral sequelae (e.g., “long COVID”)
- Signature-based response predictions to vaccinations and cancer immunotherapies
- Research tool to study HSPC biology, hematopoiesis, immune response to infection, vaccine design
- “Epigenetic vaccines” that reprogram HSPCs

Technology Advantages

- Non-invasive, based on a standard blood draw
- High resolution detection of diverse HSPC subsets
- Can be combined with single cell assays or high-throughput clinical assays (immunoassay, PCR)
- Can be scaled up for clinical applications

Supporting Data / Figures

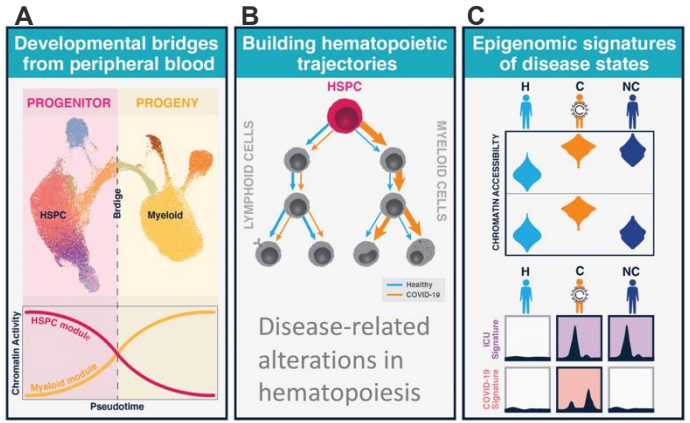

Figure 1: Proof of concept application of PBMC-PIE to a cohort of COVID-19 patients and controls recovers the developmental trajectory of myeloid cells originating from **(A)** HSPCs, **(B)** identifies disease-related alterations in hematopoiesis, and **(C)** reveals epigenetic signatures of HSPCs associated with disease states.

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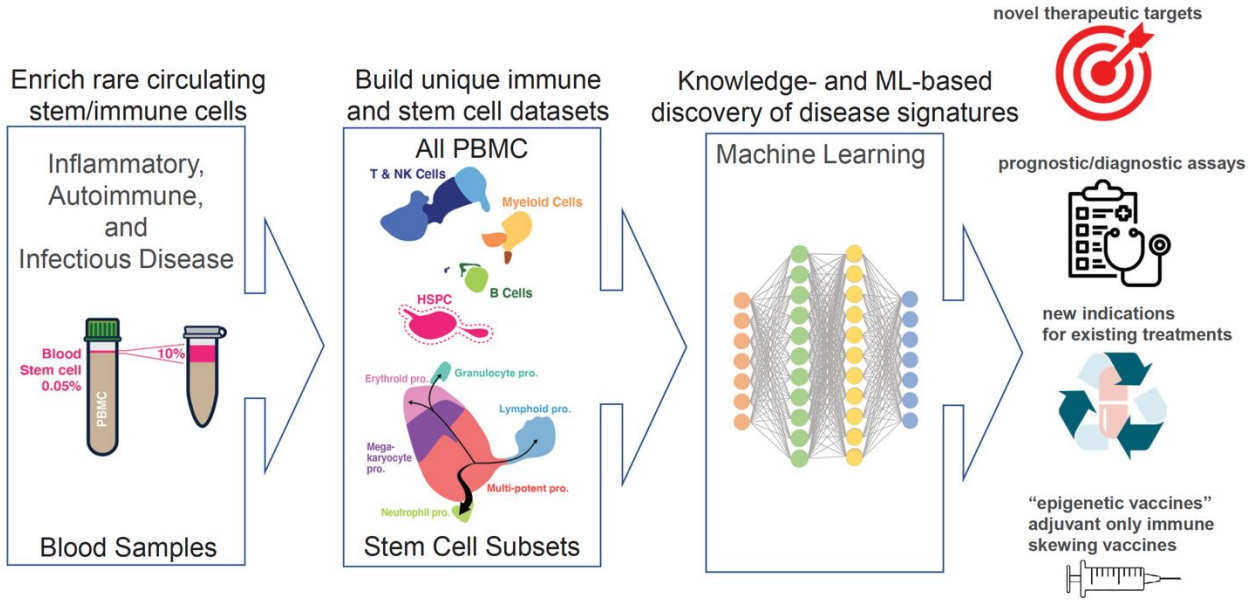

Figure 2: Schematic of PBMC-PIE workflow from HSPC enrichment and analysis to the application of machine learning approaches to discover novel therapeutic targets, design clinical assays, and develop "epigenetic vaccines"

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