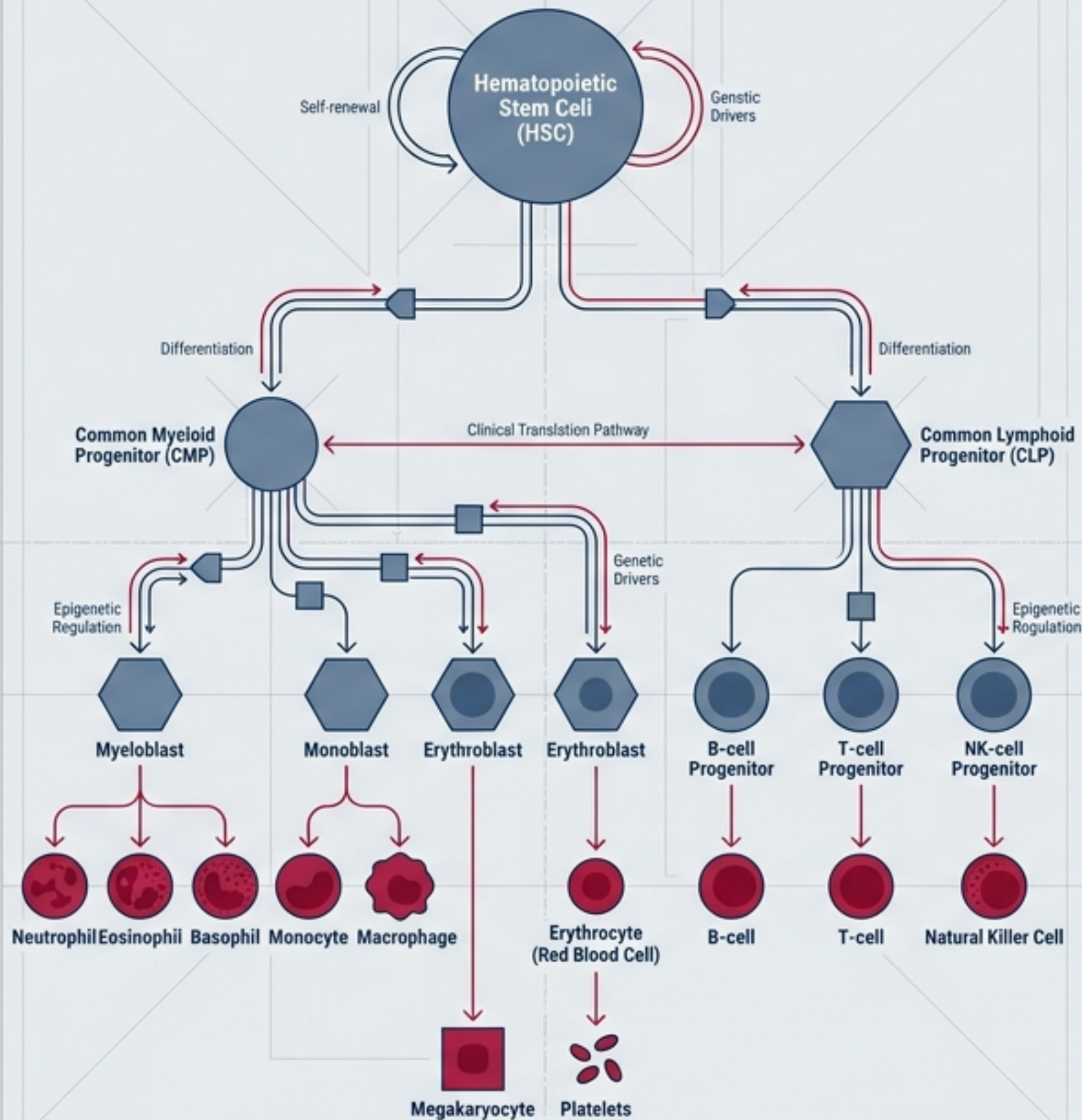


# The Sauvageau Lab: 30 Years of Translational Hematology



Pioneering the genetic and epigenetic control of stem cells, redefining AML, and translating discoveries into global clinical trials

## Human Hematopoietic Stem Cells (HSCs)

Basic Biology



Ex vivo Expansion



Clinical Gene Editing

123+ patients transplanted internationally.

## Acute Myeloid Leukemia (AML) & Solid Tumors

The Leucegene Program



Multi-omics

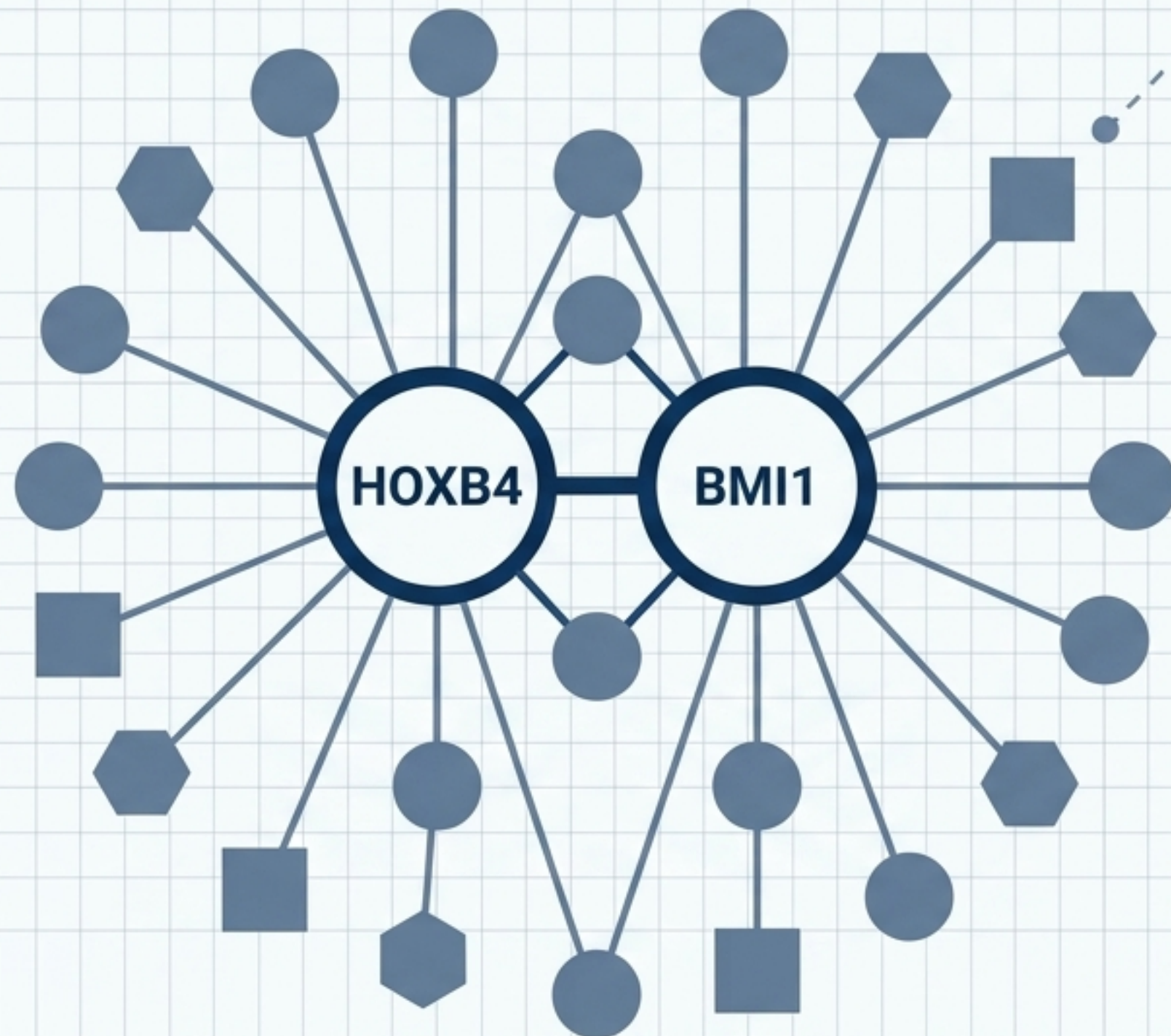


Drug Discovery

~700 primary AML specimens mapped.

Mentorship Legacy: Over 132 global trainees mentored over 30 years.

# Defining the Framework of HSC Self-Renewal



## The Pioneers

Identification of HOXB4 and polycomb gene BMI1 as essential regulators for normal and leukemia stem cells.

## The Genetic Screen

Discovery of 19 distinct nuclear factors and chromatin modifiers driving expansion via genetic screens on primary mouse HSCs.

## The Mechanism

Uncovering the central roles for asymmetric cell division factors and establishing the foundational network of stem cell biology.

# From Screen to Clinic: The UM171 Breakthrough

## Phase 1: Chemical Screen

Collaborative screening for human umbilical cord blood HSC expansion at IRIC.

## Phase 2: Discovery & Optimization

Identification and nanomolar optimization of UM171 (Science 2014).

## Phase 3: Global Clinical Trials

Phase I/II trials led with Dr. Sandra Cohen; 123+ patients transplanted with accelerated engraftment.

## Phase 4: Regulatory Approval

EMA approval (Aug 25, 2025) and creation of the ExCellThera spin-out for patients lacking optimal donors.

**Clinical benefits beyond expectations:** Modified grafts show accelerated engraftment alongside profound stem cell rejuvenation.

# Unlocking the Mechanism for Clinical Gene Editing



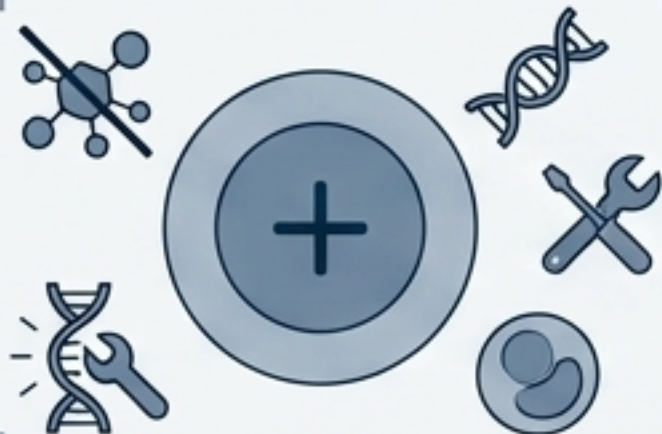
## Step 1: Receptor Binding

[1] UM171 binds to the novel E3 ligase adaptor KBTBD4.



## Step 2: Protein Degradation

[2] This complex drives the targeted degradation of CoREST1 and MYC.



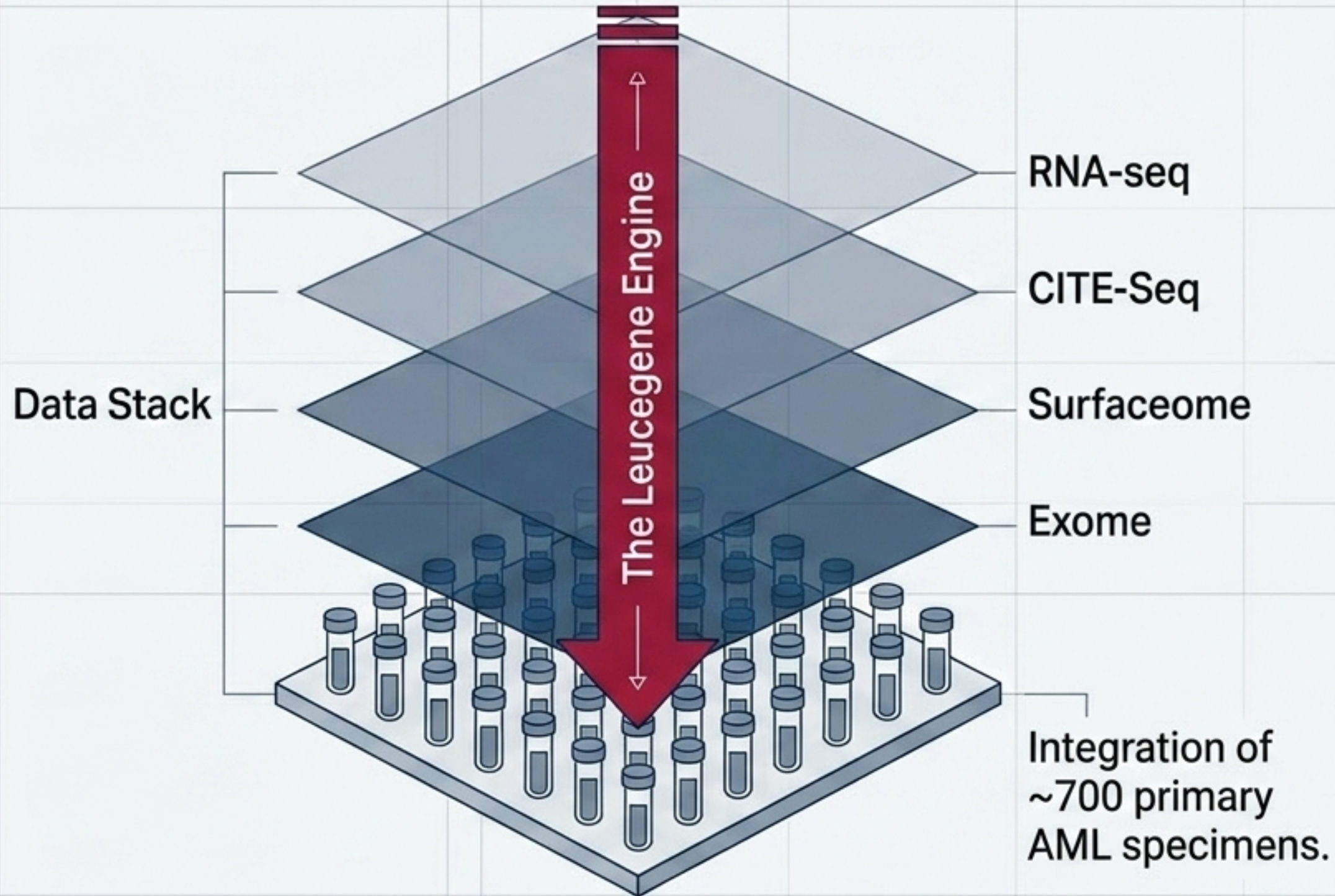
## Step 3: Cellular Restoration & Reconstitution

[3] Results in ROS clearance, DNA repair, and preservation of young HSC functions, favoring polyclonal reconstitution.

## Translational Impact

- **Sickle Cell Disease:** UM171 significantly enhances the engraftment of gene-modified HSCs.
- **Base Editing:** Enables near-complete CD33 de-epitoping, proving ideal for clinically relevant genetic manipulation.

# The Leucegene Program: Multi-Omic AML Characterization

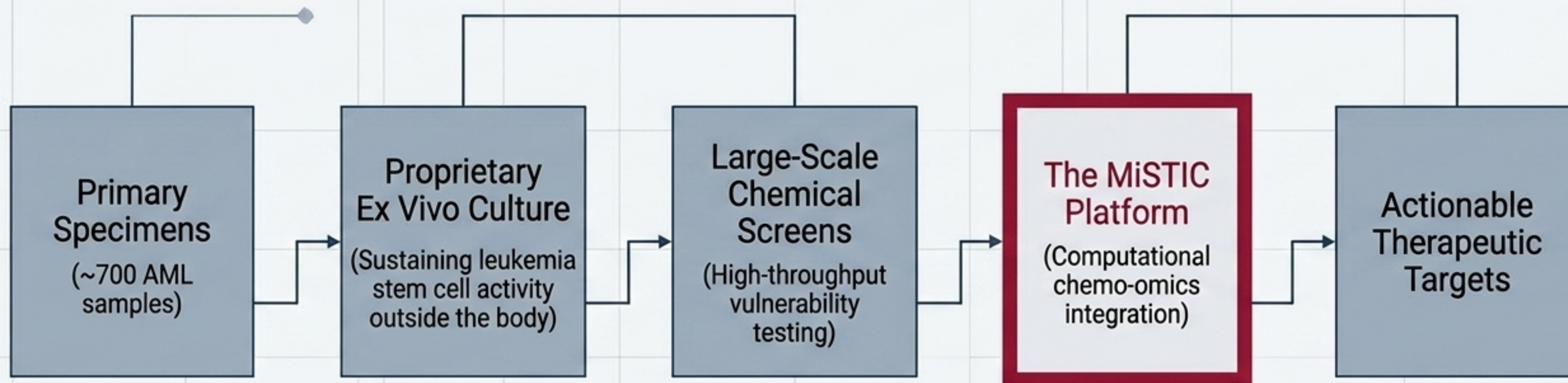


Building one of the world's best-characterized AML datasets to uncover novel diagnostic and prognostic mutations, and identify unexploited therapeutic surface targets.

# Decoding AML Genomic Signatures

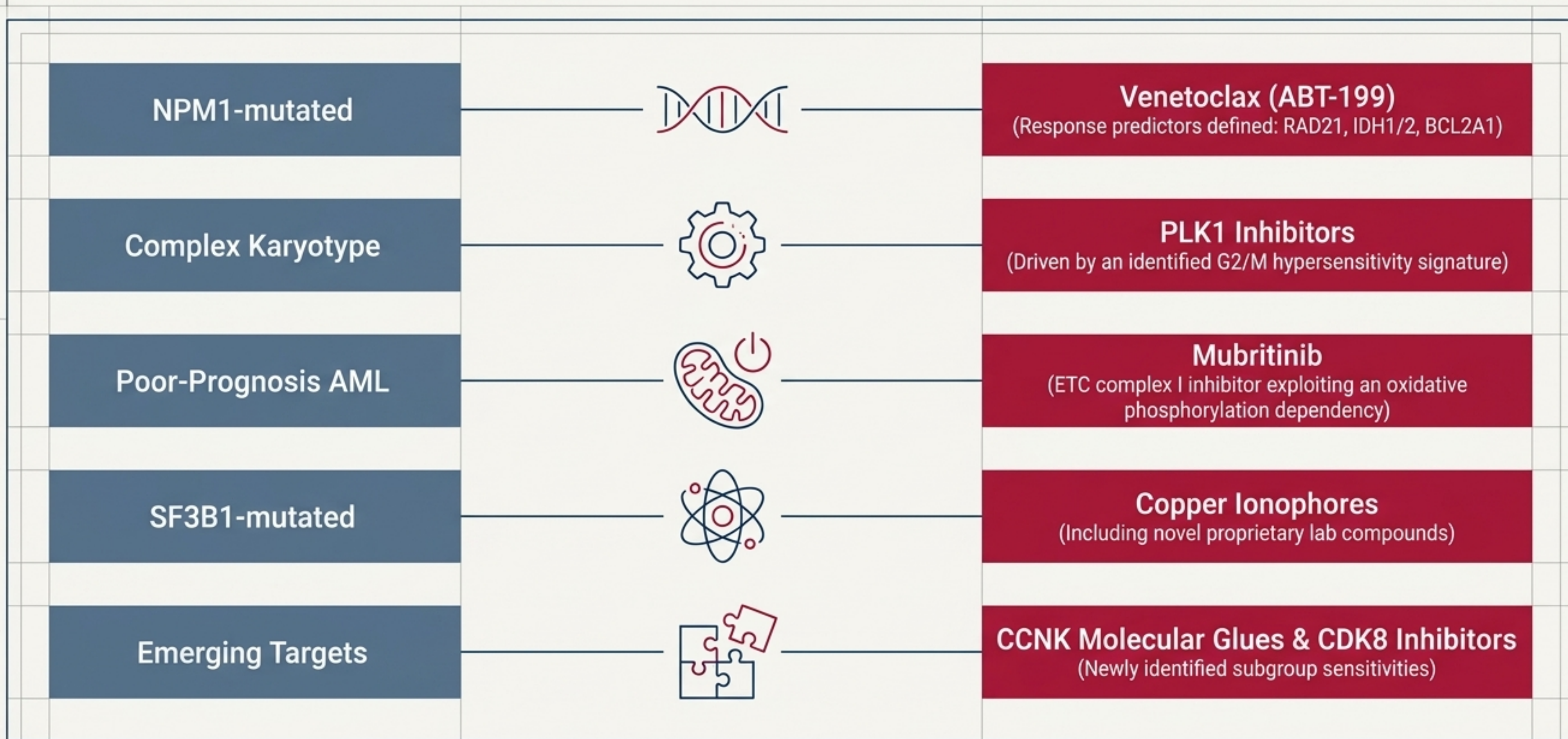
Diagnostic Table		
AML Subgroup	Unifying Marker	Clinical Implication
MLL-rearranged AML	<i>SPI1/RAS</i> mutations	Defines a unifying genetic network.
Acute Promyelocytic Leukemia (APL)	Podoplanin	Highly specific marker and primary driver of APL <b>coagulopathy</b> .
<i>RUNX1</i> -mutated AML	Allele dosage & germline variants	Dictates glucocorticoid sensitivity (now adopted clinically).
<i>TP53</i> -mutated AML	Small 3p chromosome deletion	Identifies a <b>ribosomopathic subgroup</b> highly responsive to protein synthesis inhibitors.

# Bridging Genomics to Therapeutics: The MiSTIC Platform

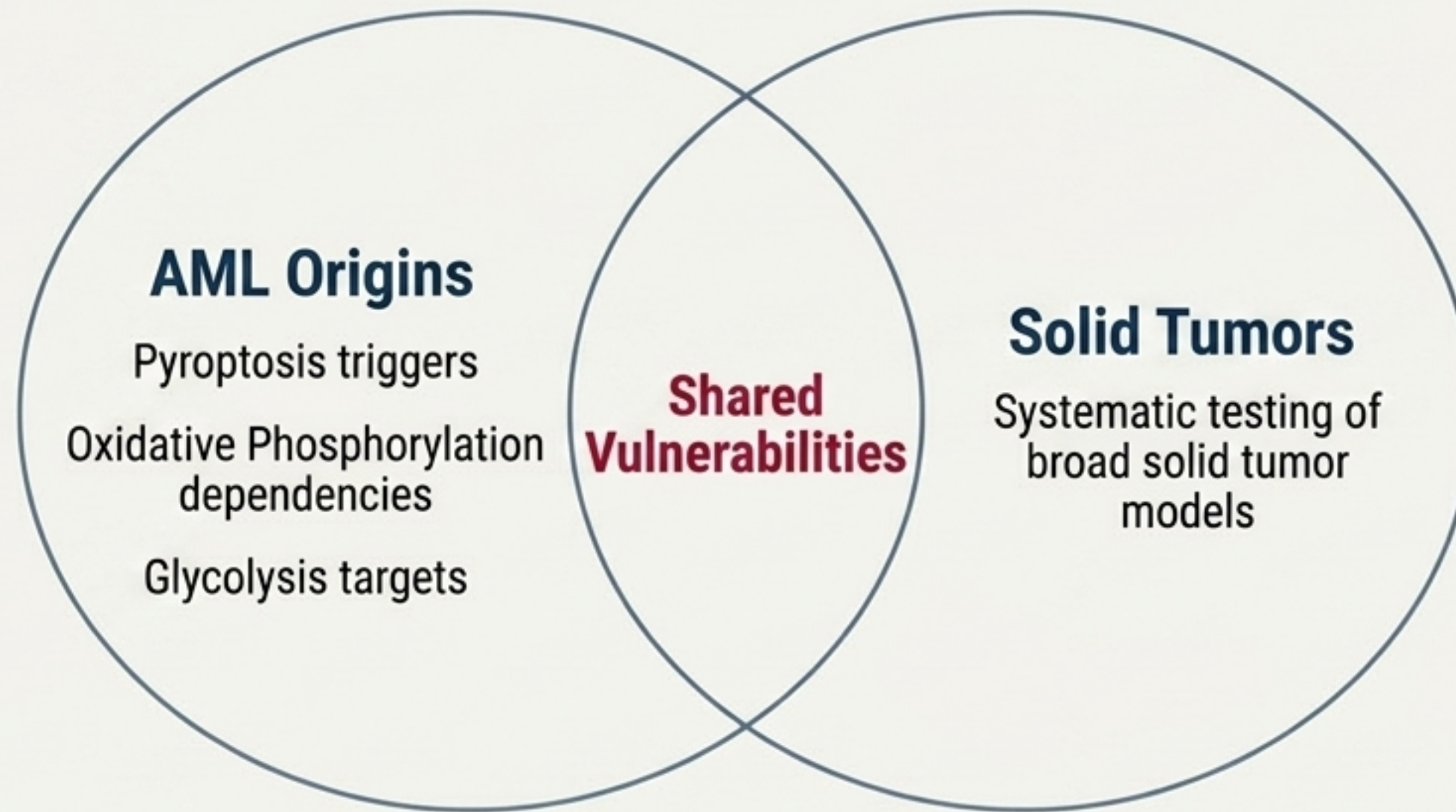


By successfully sustaining leukemia stem cells *ex vivo*, we enabled biologically accurate chemical screening that directly correlates drug response with genomic and transcriptomic profiles.

# Mapping Chemical Vulnerabilities in AML

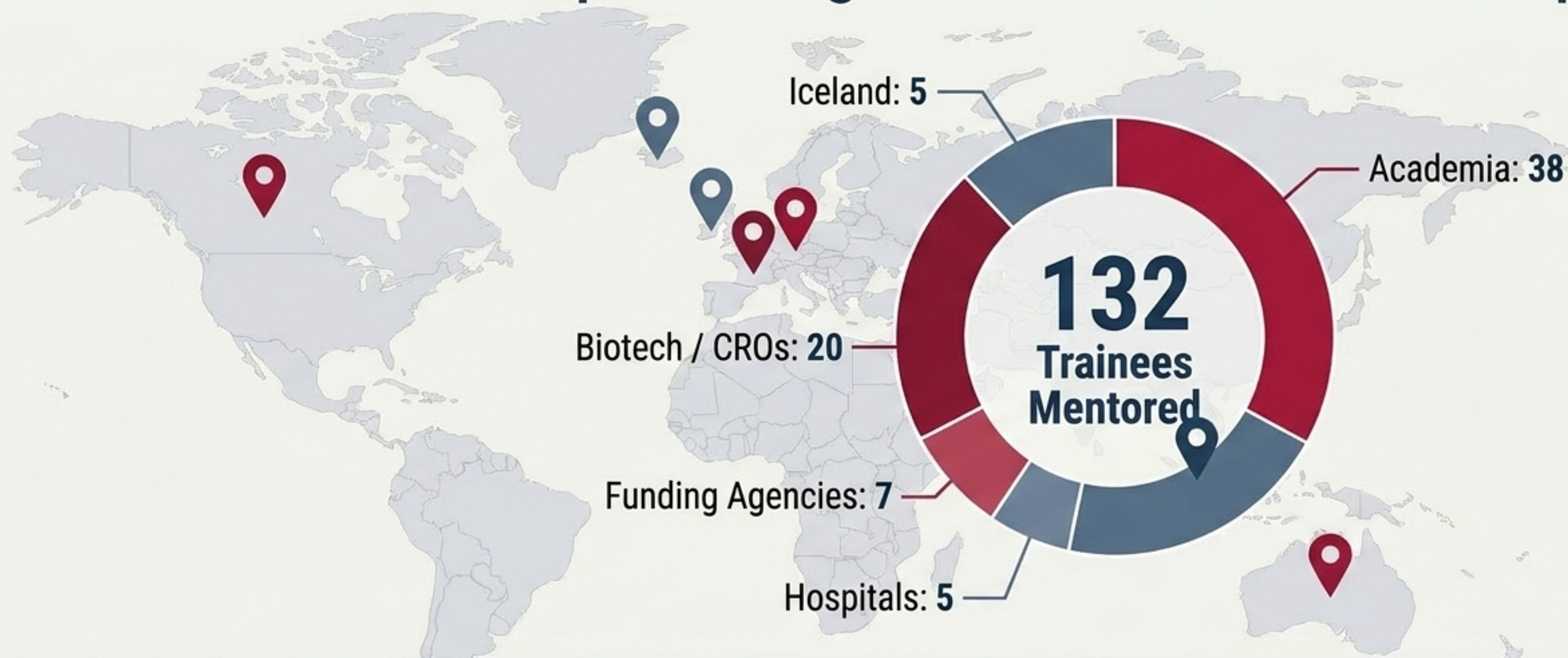


# Expanding Horizons: From Blood to Solid Tumors



Therapeutic targets uncovered in AML are actively operative in broader oncology. Novel inhibitors targeting OXPHOS and glycolysis are now in advanced stages of preclinical development for solid cancers, establishing a robust translational bridge.

# 30 Years of Mentorship: Seeding Global Science Leadership



# Advancing Science. Transforming Patient Care.

From mapping the fundamental epigenetic control of stem cells to bringing UM171 to global clinical trials, the Sauvageau Lab remains dedicated to discovering actionable vulnerabilities in cancer and engineering the future of hematopoiesis.

For collaboration inquiries, publications, and post-doctoral opportunities, please contact the laboratory directly.

