

# Computational Drug Repurposing Approaches for Identifying Novel Therapeutics Against Leukemia Subtypes

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## DESCRIPTION

Drug repurposing has emerged as one of the most compelling and pragmatic strategies in the evolving landscape of leukemia treatment. While traditional drug development remains the backbone of therapeutic innovation, the increasing complexity, cost and timelines associated with creating new agents have prompted clinicians and researchers to look toward existing drugs with renewed interest. The momentum behind drug repurposing reflects a fundamental shift in how the medical community views cancer therapeutics, emphasizing adaptability, efficiency, and scientific creativity. The rationale for drug repurposing in leukemia stems from the increasingly sophisticated understanding of leukemogenesis. Advances in genomics, proteomics, and cellular biology have revealed that leukemia is not a single disease but a constellation of biologically distinct subtypes driven by a wide array of molecular abnormalities. This heterogeneity means that a therapy designed for one specific target may unexpectedly intersect with pathways found in leukemia cells. Many drugs approved for non-oncological conditions influence signaling cascades, metabolic processes, or immune pathways that are, upon deeper analysis, also relevant to malignant hematopoiesis.

One of the major appeals of drug repurposing is its potential to overcome resistance to standard therapies. Resistance remains one of the most stubborn barriers in leukemia management, particularly in relapsed or refractory disease. Traditional chemotherapeutics and even targeted therapies can eventually fail as leukemia cells adapt, mutate, or utilize compensatory pathways. Repurposed drugs often target distinct cellular mechanisms that are not addressed by conventional leukemia treatments. This difference makes them valuable candidates for combination strategies, where they can help overcome resistance by hitting additional vulnerabilities. Furthermore, drugs that modulate metabolism, immune responses, or oxidative stress may weaken leukemic cells in ways that sensitize them to existing therapies.

Some of the most striking examples of repurposing success in leukemia come from unexpected therapeutic classes. Metformin, widely known as an antidiabetic agent, has drawn attention for its ability to impact cellular metabolism. Leukemia cells, especially those with stem-like features, exhibit altered metabolic dependencies that render them vulnerable to metabolic modulation. Metformin's inhibition of mitochondrial oxidative phosphorylation has been shown to reduce leukemia cell viability and enhance the effect of chemotherapy in preclinical studies. While the drug is not yet a standard component of leukemia therapy, its strong safety profile and extensive clinical experience make it an appealing candidate for future trials. Similarly, statins commonly prescribed to manage hyperlipidemia have demonstrated anti-proliferative activity by disrupting cholesterol synthesis pathways critical for leukemic cell membrane integrity and signaling.

In the immunologic domain, repurposing takes on another layer of significance. Leukemia is profoundly influenced by the host immune system, and drugs that modulate immune responses can have meaningful therapeutic effects. Thalidomide and its derivatives offer a well-known example of how a drug with a complicated history found new life in hematologic malignancies. Initially used for nausea and later pulled from the market due to teratogenicity, thalidomide was eventually explored for its immunomodulatory properties and became a cornerstone therapy for multiple myeloma. Although its role in leukemia is less pronounced, similar immunomodulatory strategies especially those involving cytokine regulation or T-cell activation may be harnessed through repurposing. The success of thalidomide in another hematologic cancer underscores that drugs once believed to have no place in oncology can become transformative when reevaluated through a modern mechanistic lens.

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