

Identification of a Potential AML Therapeutic Compound from an in vitro Screen

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Acute Myelogenous Leukemia (AML), the most common type of acute leukemia among adults, consists of premature leukocytes that do not fully differentiate from stem cells or immature hematopoietic cells. Ideal therapeutics would lift this differentiation block, allowing cells to fully mature. Current treatment options for AML are toxic and yield a 33% 5-year survival rate. To identify potential, new AML therapeutics, a cell-based screening process was applied to a compound library. The HL60 (AML) cell line was used to test 1040 candidates to determine if the compounds would induce differentiation. Cells at a standard concentration were aliquoted in 96 well plates, and each compound tested separately. Treated cells were incubated for 4 days, then assayed for differentiation. This preliminary work identified nine compounds that induced strong differentiation; they were then tested on OCI-AML3 cells. The compound 5H7 yielded 64% differentiation compared to 25% in a positive control. In the HL60 cells, 5H7 yielded 76% compared to 33%. HL60 cells treated with 5H7 were then tested for CD14 expression, indicating differentiation, by using flow cytometry; 90.17% of a cell surface marker of a type of mature cells was observed in 5H7 treated cells versus the positive control at 25.0%. To test cell viability, healthy leukocytes were treated with 5H7 and stained with Trypan Blue. 16% of treated cells were positive for Trypan Blue, compared to 13% of untreated cells. This suggests 5H7 is not toxic and has potential as an AML therapeutic. Future work will focus on determining mechanism of action.

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