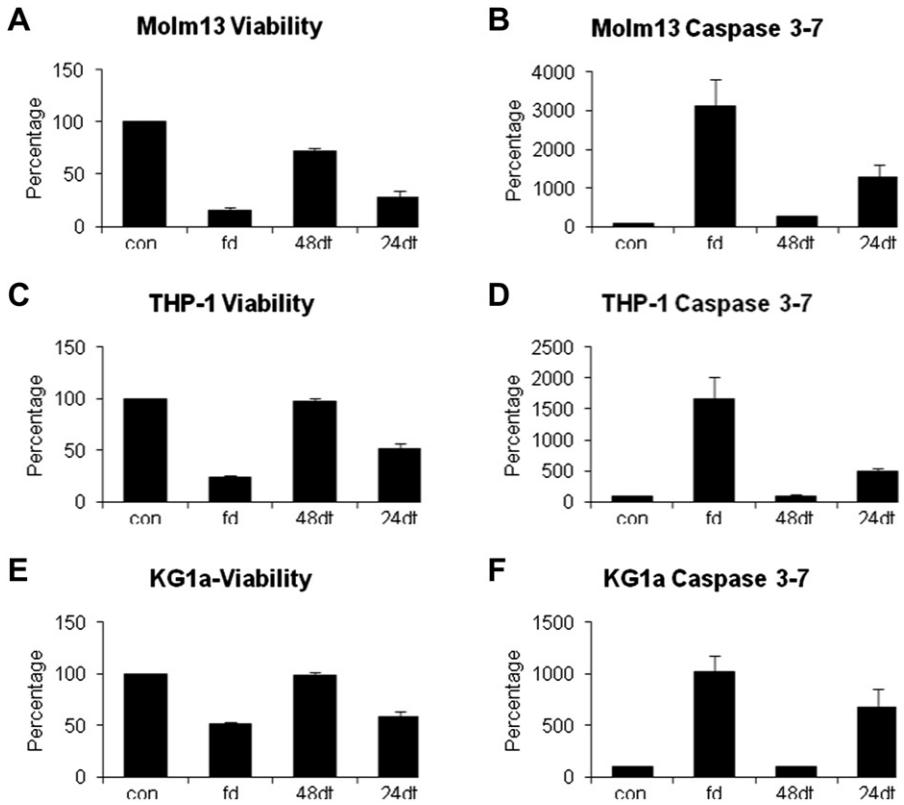
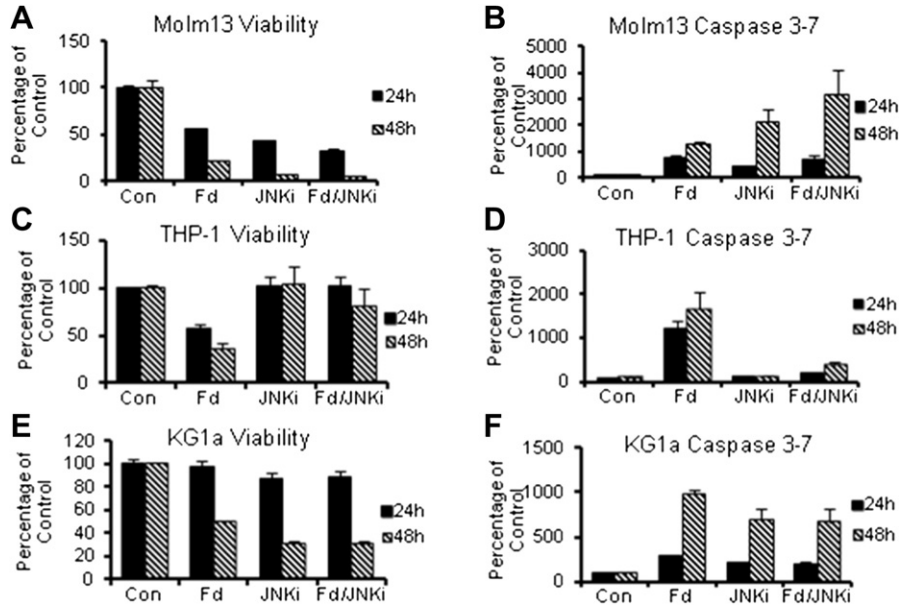
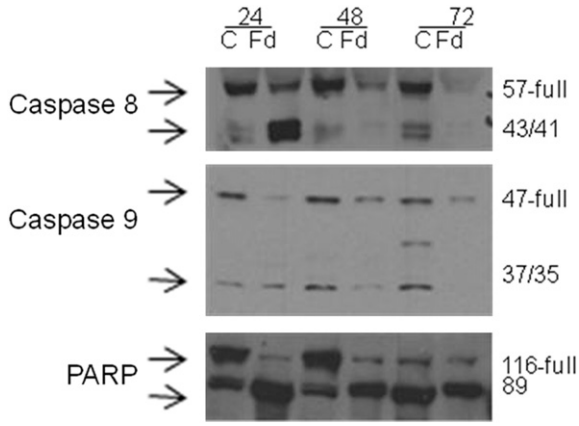


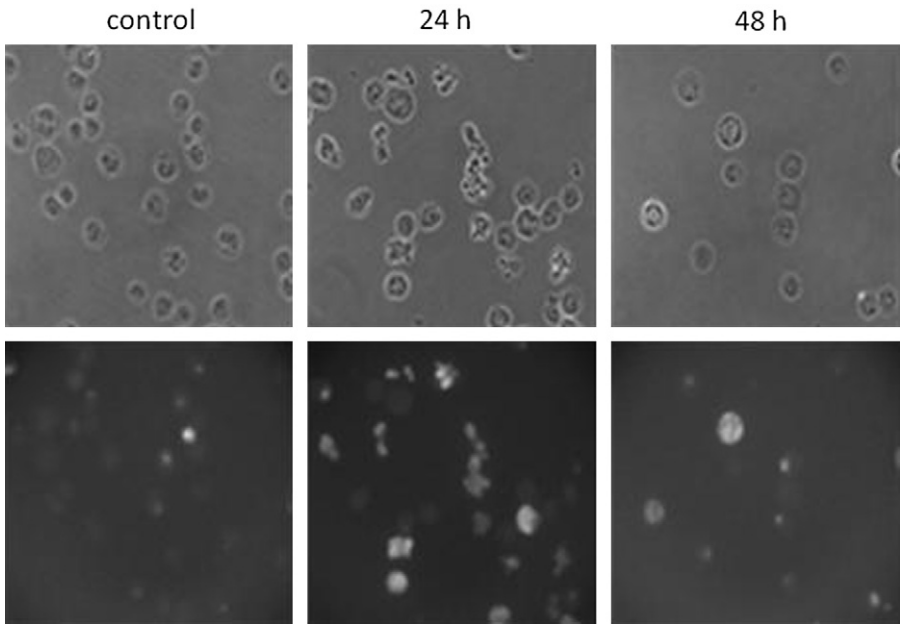
Supplementary Figure E1. FdUMP[10] (10nM) decreases viability and induces apoptosis in Molm13 (**A,B**), THP1 (**C,D**), and KG1a (**E,F**) AML cells. FdUMP[10] displays strong potency to a variety of AML cells. Assayed at 48hrs with or without addition of thymidine (dT) for the times indicated. Thy rescue for 48 h was significant ($p < 1.5$ e-7 for viability; $p < 3$ e-5 for apoptosis).



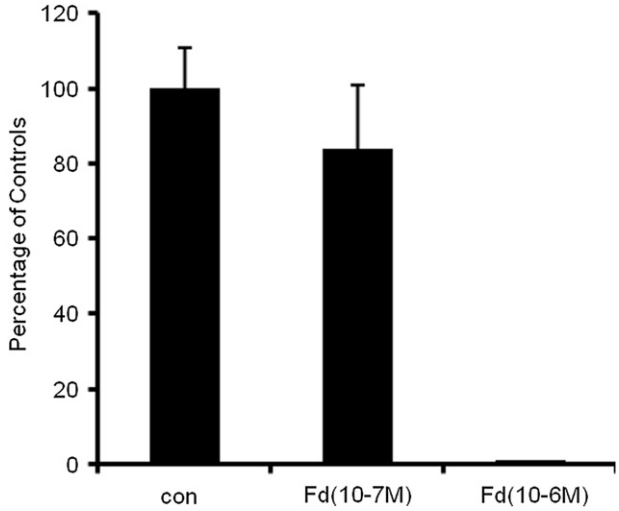
Supplementary Figure E2. FdUMP[10] (10 nM) induced apoptosis in Molm13 (**A,B**), THP1 (**C,D**), and KG1a (**E,F**) AML cells. Apoptosis is blocked by Jnk inhibition (SP600125 10 μM) in THP-1 cells (significant at 24 ($p < 0.0003$) and 48 h ($p < 0.004$) – based on eight observations) as in HL60 cells but is not significantly changed in wt p53 Molm13 cells.



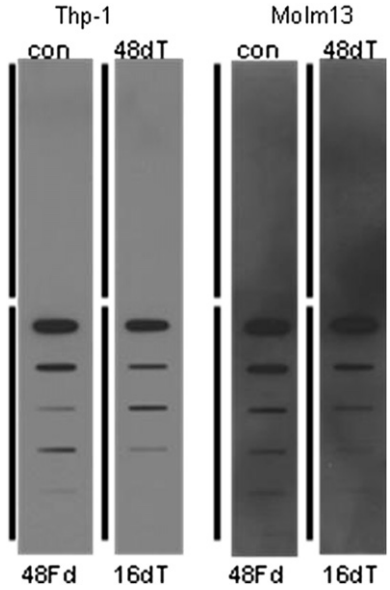
Supplementary Figure E3. WB showing FdUMP[10] treatment (10 nM) for times 24 h or longer results in cleavage of caspase 8 and 9 as well as PARP cleavage, consistent with activation of both the intrinsic and extrinsic apoptotic pathways in HL60 cells.



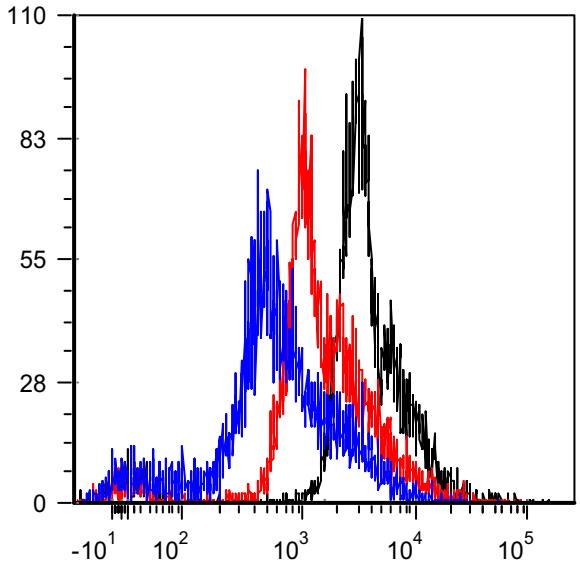
Supplementary Figure E4. Immunofluorescence images demonstrating that cleaved caspase3 is present in the majority of HL60 cells following treatment with 10 nM FdUMP[10] for 24 h (lower middle) and 48 h (lower right). Few control (vehicle-only) HL60 cells display cleaved caspase 3 (lower left). Bright field images of the same fields across the top.



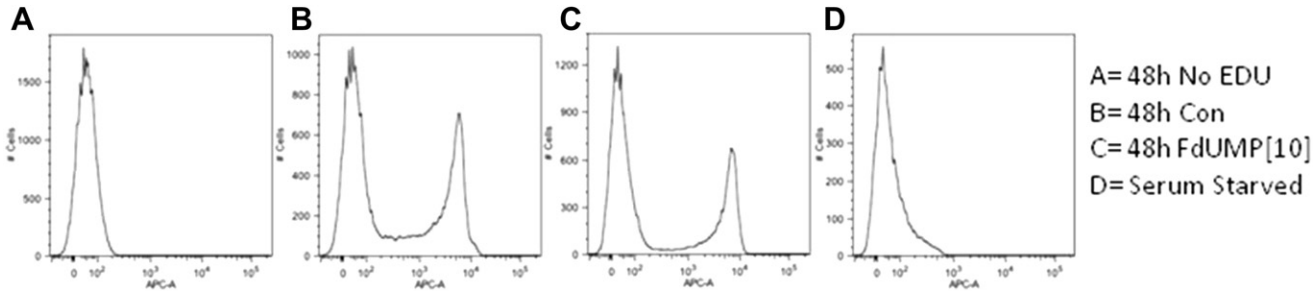
Supplementary Figure E5. Graph of concentration dependence of TS activity in Molm13 treated with vehicle-only (con) or FdUMP[10] at 1-10 μM for 24 h. FdUMP[10] strongly inhibited TS in THP-1 and KG1a cells at 0.1 μM, but required 1 μM for effective significant inhibition vs control in Molm13 cells ($p < 0.005$ based on at least five observations).



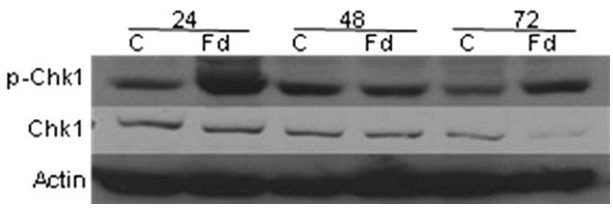
Supplementary Figure E7. ICE bioassays detecting Top1CC formed in THP1 and Molm13 cells following treatment with FdUMP[10] for 48 h or with 32 h thymidine rescue (16dT).



Supplementary Figure E6. Time-dependence of fluorescence intensity for HL60 cells incubated with Cell-trace (Invitrogen) determined by flow cytometry. The mean fluorescence intensity after 24 h (red) and 48 h (blue) is less than 0.5 and 0.25 times the initial value (black) consistent with HL60 cells replicating and dividing <20 h.



Supplementary Figure E8. Flow cytometry analysis of EdU incorporation into DNA for HL60 cells (**A**) no EdU in control cell; (**B**) Control cells with EdU treatment for 3 h - the right-shifted peak is due to newly synthesized DNA in which EdU has been incorporated; (**C**) Cells treated with FdUMP[10] for 48 h which DNA histogram analysis indicate are predominantly in G1- a similar amount of EdU is incorporated as for the control cells; (**D**) Cells synchronized in G0/G1 by serum starvation- these cells display very little EdU incorporation.



Supplementary Figure E9. Western blot showing activation of Chk1 (pS345) 24 h following FdUMP[10] treatment.