Reagents
Kinin riboside (K3000, KR), etoposide (E1383, Etop), mitoxantrone (M6545), cytarabine (C6645), 5-iodotubericidin (I100, 5-ITu), A-134974 (A2846), S-4-Nitrobenzyl-6-thioguanosine (861669, NBGT), S-4-Nitrobenzyl-6-thioinosine (N2255, NBTTI), diprydamole (D9766, DiPy), P1-P2-Di(adenosine-5') pentaphosphate pentasodium (D4022, Ap5A), fetal bovine serum (FBS), 2-mercaptoethanol, and mouse anti-GAPDH antibody (G8795) were obtained from Sigma-Aldrich (St. Louis, MO). KR was also obtained from Acros Organics (226511000; Morris Plains, NJ), Research Organics (10852; Cleveland, OH), and MP Biomedicals (102118; Solon, OH).

ABT-702 (#2372), A438079 (#2972), SQ22536 (#1435), Compound C (aka dorsomorphin dihydrochloride) (#3093), AICAR (#2840), metformin hydrochloride (#2864), PI 103 hydrochloride (#2930), and compound 401 (#3271) were from Tocris Bioscience (Ellisville, MO). Parthenolide (T113, PTL) and rapamycin (A275) were from Biomol (Plymouth Meeting, PA). Libraries (LOPAC, Sigma-Aldrich, St Louis, MO; Prestwick, Prestwick Chemical, Washington DC; Spectrum, Microsource Discovery, Gaylordsville, CT) were purchased and maintained in DMSO by the S.M.A.R.T. facility at Mount Sinai Hospital (Toronto, ON). Alamar Blue was from AbD-Serotec (Raleigh, NC). Cytokines used in tissue culture were obtained from Amgen (Thousand Oaks, CA) or from Peprotech (Princeton, NJ). Human adult plasma was obtained with informed consent (University Health Network, Toronto, ON). Methylocelulose, StemSep Human Progenitor Enrichment Cocktail, and BIT-9500 were from Stem Cell Technologies (Vancouver, BC, Canada). Low-density lipoproteins and N-acetylcysteine were from EMD Chemicals (Gibbstown, NJ). MEM, IMDM, L-glutamine, penicillin-streptomycin (Pen/Strep), CM-H2DCFDA (C6827, DCF), monobromobimane (M20381, mBBr), tetramethylrhodamine methyl ester (T668, TMRM), and Alexa 350 conjugated donkey anti-goat IgG (A-21081) were from Invitrogen (Carlsbad, CA). FACS antibodies used included: FITC-Annexin-V (BD 556419), FITC-mouse anti-BrdU (BD 556028), CD15-FITC (BD 347423), CD19-PE (BD 349209), CD38-PE (BD 347687), CD14-PE (Coulter IM0650U), CD73-PE (BD 550257), CD38-PE-Cy5 (Coulter IM2651U), HLADR-PE-Cy5 (BD 555813), CD33-PE-Cy7 (BD 333946), CD44-FITC (BD 555478), CD45 PE-Cy7 (BD 557748), APC-Annexin-V (BD 550474), CD34-APC (Coulter IM2472U), CD39-APC (BD 560239), CD45-APC-Cy7 (BD 348795), and CD123-PE (BD 555644). BrdU (550891), propidium iodide, 7AAD, and non-tissue culture treated flat-bottom 24-well or 96-well plates (351147 or 351172) were from BD Biosciences (San Jose, CA). Alexa-488 conjugated cleaved caspase 3 (9669), Alexa-488 conjugated phospho-histone H2A.X (clone 20E3, #9719), AMPK-α (2532), and phospho-AMPK-α (Thr172) (clone 40H9, #2535) were from Cell Signal Technology (Danvers, MA). Complete mini protease inhibitors and DNase were from Roche (Laval, QC, Canada). BCA protein assay kit and 10% Tris-HEPES-SDS Precise gels were from Pierce (Rockford, IL). Immobilon-P membrane was from Millipore (Billerica, MA). Mouse anti-p53 (sc-126; clone DO-1), mouse anti-Bcl2 (sc-509; clone 100), and goat anti-ADK (sc-23360, D21) were from Santa Cruz (Santa Cruz, CA). Enhanced chemiluminescent detection kit, HRP-conjugated sheep anti-mouse (NA931V), HRP-conjugated donkey anti-rabbit (NA934V) were from Amersham Biosciences (Piscataway, NJ). X-Omat Blue XB-1 film was from Kodak (Waltham, MA).

Cell culture
HL60, K562, NB4, THP1 cells were maintained in IMDM, 15% FBS, 2mM L-glutamine, 1% penicillin-streptomycin. TEX cells were maintained in IMDM, 15% FBS, 2 mM L-glutamine, 1% Pen/Strep, 20 ng/mL SCF, 2 ng/mL IL3. M9-ENL1 cells were maintained in MEM, 20%
FBS, 5% human adult plasma, 2mM L-glutamine, 1% Pen/Strep, 100 ng/mL SCF, 10 ng/mL IL3, 5 ng/mL IL7, 5 ng/mL FLT3-ligand. Primary AML and chronic myelogenous leukemia (CML) cells were cultured in IMDM, 10% BIT-9500, 5 mg/mL low-density lipoproteins, 55 µM 2-mercaptoethanol, 2 mM L-glutamine, 1% Pen/Strep, 100 ng/mL SCF, 100 ng/mL FLT3-ligand, 20 ng/mL G-CSF, 20 ng/mL IL6, 50 ng/mL TPO, 20 ng/mL IL3, 20 ng/mL GM-CSF. Lineage depleted human umbilical cord blood (Lin− CB) cells were cultured in IMDM, 10% BIT-9500, 5 mg/mL low-density lipoproteins, 55 µM 2-mercaptoethanol, 2 mM L-glutamine, 1% Pen/Strep, 100 ng/mL SCF, 100 ng/mL FLT3-ligand, 20 ng/mL G-CSF, 10 ng/mL IL3, 15 ng/mL TPO.

**Primary cells**

Primary human AML and CML cells were isolated from peripheral blood according to procedures approved by the University Health Network Research Ethics Board (Toronto, ON, Canada) and frozen viably. Cord blood (CB) samples were obtained according to procedures approved by the University Health Network and Trillium Hospital (Mississauga, ON, Canada) Research Ethics Boards. CB samples were pooled and Lin− CB cells were purified as described previously. For each leukemia or Lin− CB sample, a frozen aliquot was thawed and slowly diluted in PBS/5%FBS/0.2mg/mL DNase, counted, and cultured in 96-well plates (Alamar Blue assays) or 24-well plates (Annexin-V or ex vivo assays).

**Methylcellulose colony formation**

4,500 primary Lin− CB cells were added to 3mL of 1.2% methylcellulose, 20% FBS, 10% plasma, 48µM 2-mercaptoethanol, 50ng/mL SCF, 5ng/mL PIXY, 20ng/mL IL-3, 20 g/mL GM-CSF, 3U/mL EPO. Compounds were added to methylcellulose for 0.1, 0.3, 1, 3, or 10 μM final concentrations. For each concentration, 1.1mL of methylcellulose, cells, and compound were plated into two 35mm tissue culture dishes. Myeloid and erythroid colonies were counted after 13 days. Colony formation was normalized to plates with no compounds.

**Alamar Blue**

For follow-up studies, cell growth was measured using Alamar Blue, which is slightly more sensitive than the MTT assay for most compounds. Cells were plated in 96-well plates in 100µL media, compounds were added within 1–2hr and cultured at 37°C with 5% CO2. For primary leukemias, 50,000 cells/well; Lin− CB, 10,000 cells/well; leukemia cell lines, 10,000 cells/well. After 3 days, 10µL Alamar Blue was added to each well (~10% vol/vol). Fluorescence was measured 16–24 hr later with a SpectraMax M2 plate reader (Molecular Devices, Sunnyvale, CA) by exciting at 530nm and reading emission at 590nm. The relative fluorescence was normalized for each plate using wells with no cells (0.0) and wells with cells and no compounds (1.0) and fit using non-linear regression in Prism.

**Microarray and bioinformatic analysis**

Actively growing TEX and M9-ENL1 cells were harvested, RNA isolated using TRIzol, analyzed using Agilent 2100 Bioanalyzer, and hybridized to Affymetrix GeneChip human genome U133A 2.0 arrays (GEO platform GPL571) using manufacture protocols. TEX and M9-ENL1 gene expression was compared to HL-60 and THP1 cells using publicly available data from the same platform (GEO series GSE16160 and GSE28185). Raw CEL files for TEX, HL-60, THP1, and M9-ENL1 were processed using Bioconductor (Affy package) via RMA.
background correction, quantile normalization, and median polishing. To account for microarray batch variation, processed data was adjusted using “ComBat” version 2 package in GenePattern (Broad Institute). Gene set enrichment analysis was performed using GSEA version 2.0 with a custom list of stem cell gene sets from the Molecular Signature Database and various published reports (Broad Institute).

Chemical synthesis of kinetin riboside monophosphate
To a solution of KR in trimethylphosphate (3.0 mL) as solvent at 0°C, was added POCl3 (209 μL, ~350 mg, 2.28 mmol). The reaction mixture was allowed to warm to RT and stirred vigorously for 1.5 hours at which time the reaction was judged complete (TLC analysis showed complete consumption of starting material). The reaction mixture was recooled to 0°C and diluted with water (3.0 mL). The mixture was adjusted to pH 5-6 with 2.5 M NaOH and extracted with CH2Cl2 (6 × 5 ml). The aqueous layer was then concentrated in vacuo to give the crude product, which was purified on C-18 silica (biovage) using acetonitrile and water as eluant to give 75 mg of a beige solid (31% yield). NMR analysis showed the expected profile: 1HNMR (400 MHz, D2O)d: 8.32 (s, 1H), 8.13 (s, 1H), 7.29 (m, 1H), 6.23 (m, 2H), 5.95 (d, 1H), 4.56 (m, 3H), 4.35 (dd, 1H), 4.24 (m, 1H), 4.00 (m, 3H); ESI-MS m/z 427.75.

Immunoblotting
Treated cells were harvested, lysed on ice in 50 mM Tris, pH 7.5, 150 mM NaCl, 1% NP40, 2mM EDTA, 1mM sodium vanadate, 1mM PMSF, Complete Mini protease inhibitors, and clarified at 14,000rpm. Protein concentrations were measured by BCA assay and 7.5μg protein/lane were separated on 10% Tris-HEPES-SDS gels in 100mM Tris/100mM HEPES/1% SDS, pH 8.0 followed by transfer to Immobilon-P (PVDF) membranes. Membranes were probed with antibodies in TBS/0.05% Tween-20/5% non-fat milk (w/v) for 60min, washed with TBST/milk, incubated with ECL Plus following manufacturer’s instructions, exposed to film, scanned and analyzed using NIH ImageJ 1.40g.

Statistical analysis
Data is presented as the mean ± S.E.M and graphed using Prism 5.0 (Graphpad, La Jolla, CA). The nonparametric Wilcoxon rank-sum test was used (Mstat 5.10, Dr. Norman Drinkwater, University of Wisconsin-Madison). Fitted curves were compared using the F-test based on sum-of-squares and degrees of freedom from separate and combined fits.
**Figure S1. Gene set enrichment analysis of TEX and M9-ENL1 cells**
Gene expression in TEX and M9-ENL1 cells was analyzed using Affymetrix HG-U133A 2.0 microarrays. Processed data was combined with published microarray data for HL60 and THP1 cells using the ‘ComBat’ package in GenePattern to adjust for batch variation. Probes were compared between cell types (i.e., TEX vs HL60, M9-ENL1 vs HL60, etc) and gene set enrichment analysis (GSEA) performed using a custom list of embryonic, adult, and cancer stem cell gene sets from published sources and the Molecular Signature Database. GSEA was also performed using the ‘curated’ (c2) gene sets (version 3.0) from the Molecular Signature Database. The normalized enrichment (NES), FDR, and p-value for each gene set are provided. Left panels: TEX (class 0) vs HL60 (class 1). Middle panels: TEX (class 0) vs THP1 (class 2). Right panels: M9-ENL1 (class 3) vs HL60 (class 1). Number of samples: TEX = 3; M9-ENL1 = 3; HL60 = 4; THP1 = 2.

**Figure S2. HTS screen of TEX and M9-ENL1 cells**
(A) TEX and M9-ENL1 cells were plated in 96-well plates, compounds (LOPAC, Prestwick, and Spectrum libraries) added within 1hr, and cultured for 72hr. 10uL (microliters) Alamar Blue was added and cell growth was measured using Alamar Blue fluorescence 24hr later. The raw arbitrary fluorescence data was normalized using untreated (100%) and media-only control (0%) wells on each plate. A B-score or Z-score (not shown) for each compound was calculated using normalized data. Hits (red dots) were identified by a B-score (or Z-score) more than 3 standard deviations (green dashed line) from the mean (blue line). The overall Z factor for TEX cell LOPAC library screen is shown. (B) Left: The number of hits from each library and cell line is shown. A total of 200 unique compounds were identified from the six screens. Some compounds were identified as ‘hits’ in all 6 screens, whereas some were identified as a ‘hit’ in only one screen. Middle panel: For each of the 200 hits, the normalized cell growth values (0% represents complete cell growth inhibition) from all available screens were combined and averaged (N=2 to N=6). By averaging all available data for each hit, only 80 compounds inhibited cell growth to 25% of control cells (red bar). Right panel: Of these 80 compounds, 76 targeted both TEX and M9-ENL1 cells (see Table S2 for a list of the top 80 compounds). 19 of the 80 compounds are known chemotherapeutic agents (red bars) and indicated in Table S2. C) To identify compounds with potential limited side effects on normal HSC and progenitor cells, 55 of the 80 compounds were tested on three separate batches of Lin¬ CB cells using the Alamar Blue assay. Three doses were tested: 5, 1.67, and 0.56µM. 25 compounds were not tested because of structural redundancy or known toxicity. Left panel: 27 (49%) of the 55 compounds showed equal toxicity between normal and leukemia cells. Aklavine HCl is presented as an example. Middle panel: 18 (33%) of the 55 compounds were more toxic to normal cells. Anthothecol is presented as an example. Right panel: 10 (18%) of the 55 compounds were more toxic to leukemia cells. Etoposide is presented as an example.

**Figure S3. Kinetin riboside and parthenolide induce apoptosis in multiple CD34 and CD38 fractions of primary AML patient samples**
Eleven primary AML samples were cultured for 16hr with DMSO vehicle (black), 10µM KR (white), or 5µM PTL (grey). The frequency of apoptotic cells in CD34+CD38−, CD34+CD38+, CD34−CD38+, or CD34−CD38− fractions is shown. * p<0.05, ** p<0.01, *** p<0.001; Wilcoxon rank sum test.
Figure S4. In vitro sensitivity of primary bulk and CD34⁺CD38⁻ AML cells to KR and PTL
(A, B) Primary AML cells (same samples as used in Fig. 4B and Table S6) were cultured in 96-well plates in the presence of kinetin riboside (A) or parthenolide (B). Growth was measured using Alamar Blue as described in Fig. 1A. (C) Primary AML cells were cultured overnight with DMSO vehicle (black), 10μM KR (white), or 5μM PTL (grey). Apoptosis was assessed by staining for CD34⁻APC, CD38⁻PE, and FITC-Annexin-V and propidium iodide. The frequency of apoptosis (Annexin-V positive) in CD34⁺CD38⁻ cells is shown. These cells were then injected into NOD/SCID mice as described in Fig. 4A.

Figure S5. Leukemic engraftment of nude/NOD/SCID mice
Human AML cells (sample #2, M2 FAB, female, age 52, trisomy 8) were IF injected into irradiated nude/NOD/SCID mice as described in Material and Methods. (A) Human engraftment in the injected right femur was quantified using human specific anti-CD45⁻APC-Cy7. (B) A fraction of CD45⁺ cells were also CD34⁺. The CD45⁺ cells were verified as myeloid leukemic based on expression of CD33⁺CD19⁻CD15⁺CD14⁺CD11b−HLADR⁻C–H). Gating was determined using mouse IgG1 isotype antibodies.

Figure S6. Kinetin riboside induces loss of mitochondrial membrane potential, cleaved caspase 3, and apoptosis
(A–F): TEX, M9-ENL1, HL60, NB4 and K562 cells were cultured overnight in the presence of kinetin riboside (KR), or etoposide (Etop) at 0.3, 1, or 10μM. Loss of mitochondrial membrane potential (TMRM negative cells) was measured by staining with TMRM and flow cytometry. Error bars = SEM, N=3. G) TEX, M9-ENL1, HL60, NB4 and K562 cells were cultured overnight in the presence of kinetin riboside (KR), or etoposide (Etop) at the indicated concentrations. Cells were stained for apoptosis (Annexin V⁺) or cleaved-caspase 3 (intracellular flow cytometry).

Figure S7. N-acetyl-cysteine (NAC) does not prevent and P2X7 activity is not required for KR-induced cell death
(A) TEX and M9-ENL1 cells were treated at the indicated concentrations of kinetin riboside (KR) or etoposide (Etop) in the presence of NAC (1mM). Apoptotic cells (Annexin-V positive) were quantified by FACS analysis. NAC did not prevent KR or etoposide induced cell death in TEX or M9-ENL1 cells. (B) TEX cells were treated with kinetin riboside (in a 2-fold serial dilution starting at 10μM) in the presence of A-438079, a competitive antagonist for P2X7, at 0.01 (squares), 0.1 (triangles), 0.5 (inverted triangles), 1 (diamonds), 5 (open circles), or 10μM (open squares) using the Alamar Blue assay. A-438079, a competitive antagonist for P2X7, the cell-surface purinoreceptor for ATP, did not prevent KR-induced cell killing at any dose indicating KR is transported into cells without phosphate modification.

Figure S8. Leukemia cell lines and primary AML cells generally lack CD73 and CD39 expression
Actively growing TEX, M9-ENL1, HL60, K562, NB4, THP1, Ramos, U937, Jurkat, or cells from 4 primary AML samples were stained for CD73 and CD39. Primary AML samples are the same as used in Fig. 4. Negative staining for each line was determined using IgG1 isotype controls (blue lines). Only AML-1 expressed CD73 whereas AML-1, AML-2, and AML-3 expressed CD39.
Figure S9. ADK levels correlate with sensitivity to KR

(A–D) TEX, M9-ENL1, HL60, and NB4 cells were fixed, permeabilized, and stained for intracellular adenosine kinase (ADK). Cells were fixed for 30min in ice-cold 1.6% PFA, permeabilized for 30min in ice-cold 90% methanol, and resuspended in 100μL PBS/3% FBS. Cells were stained for 60min at room temperature with 100ng (in 5μL) goat anti-ADK. Cells were analyzed on a LSRII and gates set based on cells stained only with secondary antibody. (E) Histogram of ADK staining for TEX (red), M9-ENL1 (blue), HL60 (green), and NB4 (orange) cells. (F–H) Correlation between ADK staining (MFI-median fluorescence intensity) and KR, etoposide, or parthenolide IC50 for TEX, M9-ENL1-HL60, or NB4 cells. Correlation coefficients are indicated on each graph. (I–K) TEX cells were cultured with DMSO vehicle or 100nM 5-ITu (ADK inhibitor) along with kinetin riboside (I), etoposide (J), or parthenolide (K). 5-ITu was only able to inhibit KR-induced cell death.

Figure S10. ADK inhibition prevents TEX cell killing by KR-monophosphate

(A) Schematic of chemical synthesis of kinetin riboside monophosphate (KR-P). See Materials and Methods above for description. (B) KR and the monophosphate derivative (KR-P) inhibited TEX cell growth as measured by Alamar Blue, but KR-P was 2.25-fold less effective than KR (0.468μM +/- 0.011 vs. 0.208μM +/- 0.003; F-distribution p-value < 0.001). (C) Inhibitors of nucleobase uptake (NBTI-red squares; NBTG-blue triangles; DiPy-green inverted triangles), adenosine kinase (ABT-702-orange diamonds; 5-ITu-pink open circles; A-134974-brown open squares), adenylate kinase (Ap5A-open yellow triangles), adenylate cyclase (SQ22536-open grey diamonds) and an adenylate cyclase activator (NKH477-open blue inverted triangles) were tested at 500nM in the presence of KR monophosphate (KR-P).

Figure S11. Investigation of AMPK signaling in TEX cells

(A) Western blot analysis of AMPK, phospho-AMPK, and GAPDH levels after overnight treatment of TEX cells with the indicated concentrations of KR, etoposide (Etop) or parthenolide (PTL). (B) AMPK and phospho-AMPK levels from (A) were normalized to GADPH. (C) TEX cells were cultured overnight in the presence of vehicle, 1μM KR, 2mM metformin, 0.5mM AICAR, or combinations of KR and metformin or AICAR. Apoptosis (Annexin V+) was measured by flow cytometry.

Figure S12. Narasin and nigericin toxicity on normal HSC and progenitor cells

Gupta et al found salinomycin, and to a lesser degree nigericin, targeted breast cancer cells engineered to undergo EMT, which acquired markers of breast cancer stem cells (i.e., CD44+CD24-). Salinomycin is structurally similar to narasin. Narasin and nigericin were identified as potent hits in primary screens on TEX and M9-ENL1 cells and selected for secondary IC50 screens. Narasin (A) and nigericin (B) were tested on TEX (black circles) and M9-ENL1 (red squares) cells in a 2-fold dilution series from 10μM to ~20nM. Three separate pools (blue triangle, green triangle, and orange diamond) of Lin- CB cells, as a source of HSC and progenitor cells, were tested at 5, 1.667, and 0.556μM using Alamar Blue. Both compounds were more sensitive on normal cells than TEX or M9-ENL1 cells and not further studied.
REFERENCES

Figure S1

TEX vs HL60

Enrichment plot: OP/TERT
NES=1.92
FDR=0.002
p=0.000

TEX vs THP1

Enrichment plot: OP/TERT
NES=1.58
FDR=0.090
p=0.006

M9-ENL1 vs HL60

Enrichment plot: NADDAD_E LYMPHOCYTE PROGENITOR
NES=2.68
FDR=0.000
p=0.000

Enrichment plot: ISHIIWA, LSC_UP
NES=1.67
FDR=0.022
p=0.010

Enrichment plot: ISHIIWA, LSC_UP
NES=1.70
FDR=0.058
p=0.014

Enrichment plot: SENPOK/MTH1/L3_SET
NES=1.66
FDR=0.089
p=0.000

Enrichment plot: GENTLES, LSC_UP
NES=1.86
FDR=0.003
p=0.000

Enrichment plot: GRAHAM_NORMAL, QUINCENT/VN/NORMAL, DIVISION
NES=1.67
FDR=0.056
p=0.002

Enrichment plot: KLEIN, TARGETS OF BCS, NB1, FUSION
NES=1.82
FDR=0.075
p=0.000

Enrichment plot: NADDAD_E LYMPHOCYTE PROGENITOR
NES=2.68
FDR=0.000
p=0.000
Figure S2

(a) Plate cells

- Add compounds within 1 hr
- Culture 72 hrs
- Add Alamar Blue
- ~24 hrs later, measure Alamar Blue

(b) Library

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<td>Total hits</td>
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Select hits based on Z-score or B-score

Top 80 hits

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<tr>
<td>Total hits</td>
<td>144</td>
<td>181</td>
</tr>
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</table>

200 unique hits

(c) Equal toxicity (27 of 55)

Lin- CB more sensitive (18 of 55)

Leukemia more sensitive (10 of 55)

- Normalized activity vs. concentration of chemicals (Alkalin HCl, Anthotheced, Etoposide)
Figure S3

The figure shows a bar chart comparing Annexin + (%) levels across different cell populations labeled as CD34+CD38- and CD34+CD38+. The chart includes three groups: CON, KR, and PTL. Statistical significance is indicated by * (p < 0.05), ** (p < 0.01), and *** (p < 0.001).
Figure S4

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

U

V

W

X

Y

Z
Figure S5
Figure S7

A

![Bar chart showing Annexin + (%) for different treatments.](image)

<table>
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<tr>
<th>Treatment</th>
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V

![Line graph showing normalized activity for different concentrations of Kinetin riboside.](image)

- **A438079**
  - ▲ 0µM
  - ▼ 0.01µM
  - ▲ 0.1µM
  - ▼ 0.5µM
  - ◇ 1µM
  - ○ 5µM
  - □ 10µM

Kinetin riboside (µM) vs. Normalized activity
Figure S8
Figure S9
Figure S10

A

\[
\text{Kinetin riboside} \quad \xrightarrow{\text{POCl}_3} \quad \text{Kinetin riboside monophosphate}
\]

B

\[
\text{Normalized activity vs. Concentration (\(\mu\text{M}\))}
\]

KR IC\text{_{50}}: 0.208 ± 0.003
KR-P IC\text{_{50}}: 0.468 ± 0.011

C

\[
\text{Normalized activity vs. Kinetin riboside monophosphate (\(\mu\text{M}\))}
\]

vehicle
NBTI
NBTG
DiPy
ABT-702
5-ITu
A-134974
Ap5A
NKH477
SQ22536
Figure S11

A

B

C

Amphoterin 5 µM

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Normalized to GAPDH

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Annexin + (%)

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<th>Metformin 2 mM</th>
<th>AICAR 0.5 mM</th>
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Diagram showing protein expression levels and Annexin V positivity.
Figure S12

(A) Graph showing normalized activity against Narasin concentration.

(B) Graph showing normalized activity against Nigericin concentration.