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Reporting Summary

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Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	flow cytometry data was acquired with BD-LSRII analytical flow Cytometer.
Data analysis	FLoJo9.3 was used to analyze Flow cytometry data, R-studio with R version 3.5.1 was used for PCA, Inveon acquisition workplace v 2.0.0.1050 and inveon research workplace v 4.1 was used for PET acquisition and image reconstruction. Prism version 6 and 7.0d were used to analyze and graph data.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the plots within this paper and other findings of this study are available from the corresponding author upon reasonable request.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences

Study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	a sample size of 10 mice per group were determined to allow 10% resolution in the survivability study.
Data exclusions	Mice we excluded from treatment analysis or survival studies prior to initiation of therapy when disease burden in peripheral blood exceeded 2 standard deviations from the cohort at initial disease burden blood draw after 4 days. Exclusion prior to therapy was to tighten disease burden thus a tighter survival and disease burden measurement once started.
Replication	in vivo samples were replicated at least twice in different cohorts of mice and successful. each cohort contained n=10 animals per treatment or control arm. survival studies that did not replicate life extension were due to over implantation of AML, or the inability to dose mice intravenously due to the numerous injections previously administered (for implantation and therapy), or a systemic infection requiring euthanasia of the entire cohort.
Randomization	animal cages were randomized prior to therapy monitoring and survival arms
Blinding	Samples and subjects (animals) were not blinded in the experiment as the iron particles are brown compared to colorless saline, and mice were organized after randomization into cages for each type of therapy thus identifying the therapy. Unblinded cages still adhered to animal welfare requirements equally and dosing schedules. However data collection analysis and exclusion criteria for disease burden were established previously.

Materials & experimental systems

Policy information about availability of materials

n/a	Involved in the study
☐	☒ Unique materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☐	☒ Research animals
☐	☒ Human research participants

Unique materials

Obtaining unique materials	Unique materials such as fluorescent or radiolabeled ferumoxytol can be easily made from commercial reagents outlined in doi:10.1038/nprot.2017.133

Antibodies

Antibodies used	Antibodies and their clone number are provided in the methods section and and detailed information is available in Supplementary Table 3 and coped below: Murine CD45 PECy5 clone:30F11 103110 Lot: B219251 Dilution 1:1000 BioLegend Human CD45 APC-Cy7 clone:2D1 368516 Lot:B224328 Dilution 1:100 BioLegend Human CD45 APCH7 clone:2D1 560178 Lot:6118754 Dilution 1:100 BD Pharmigen Human CD34 PECy7 clone:581 560710 Lot:7054753 Dilution 1:100 BD Pharmigen Human CD38 APC clone:HIT2 555462 Lot:55114 Dilution 1:100 BD Pharmigen Human Ferroportin AF405 clone:8G10NB NBP2-45356 Lot:A-3-101717 Dilution 1:50 Novus Biologicals Isotype IgG2b AF405 MCP-11 NBP2-27231 Lot:AB100711A-6-042518 Dilution 1:50 Novus Biologicals
Validation	Antibodies and their clone number are provided in the methods section and can be traced to the manufacturers website for validation. antibodies were titrated based on recommended concentrations prior to flow experiments to determine optimal signal sensitivity and run with isotype controls.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Cell lines used are found in Supplementary Information Figures 1 and 2. Cell lines were acquired from ATCC, while patient derived cell lines were obtained directly from patients with IRB approval of both Weill Cornell Medical College and Memorial Sloan Kettering Cancer Center. Cell lines used in this manuscript: HL60, KG-1, KCL22, UKE-1, MV411, REH, ME-1, KASUMI-1, U-937, THP-1, OCI-AML2, SET-2, MOLM13, K562, HEL, TF-1, TUR, SKM-1, OCI-AML3, SKNO-1
Authentication	Cell lines were authenticated by STR profiling
Mycoplasma contamination	Myoplasm testing was done on cell lines and is found in the methods section under cell lines. cell lines were found to be negative for mycoplasm.
Commonly misidentified lines (See ICLAC register)	U-937 is listed as a misidentified cell line. Use of this line was limited to the initial staging of leukemias as low in FPN gene and protein expression.

Research animals

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Animals/animal-derived materials	c57black6j female mice 4-6 weeks old were used for all in vivo and survival studies in Figures 1 and 2 and obtained from Jackson laboratories. For patient derived xenografts in Figure 3, Nod-SCID 4-6 week old female mice from Jackson laboratories were used.

Human research participants

Policy information about studies involving human research participants

Population characteristics	IRB approval was obtained from Weill Cornell Medical College-New York Presbyterian Hospital and from the University of Rochester Medical Center and described in the methods section. informed consent was obtained from all individuals. patient population covered acute myeloid leukemias, with the following known characteristics: AML2 M4; Normal cytogenetics; Relapsed, AML4 De Novo; M2; Normal cytogenetics, AML5 MDS progression to AML, AML10 del(9)(q13)[1]; De Novo, AML12 De Novo; Normal cytogenetics, AML14 MDS progression to AML, AML15 Refractory; 4, XY, +8[3], AML18 Normal cytogenetics; FLT3-ITD+, mut/NPM1; De Novo, AML20 FLT3-ITD+, AML34 NPM1 type A, AML37 Relapsed, AML72 NPM1 type A, AML74 NPM1 type A, AML75 NPM1 type A, AML91 FLT3 wt, NPM1 wt. No additional population characteristics are readily available.

Method-specific reporting

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ Magnetic resonance imaging

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Samples were washed twice in PBS as detailed in Methods section
Instrument	A BD LSR II was used for all flow cytometry acquisition
Software	flow cytometry data was acquired and plotted in FloJO v 9.3 or later.
Cell population abundance	for in vitro, 2 million cells in culture were treated for the described time and then all cells were run by flow to determine fate and viability. For in vivo studies 100uL of peripheral blood were used per measurement. For bone marrow and spleen 1/10 of the collected samples were run on flow. The same gating strategy was used for all samples.
Gating strategy	The gating strategy is depicted in supplementary figures 1-3, and described in detail in the methods section

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.