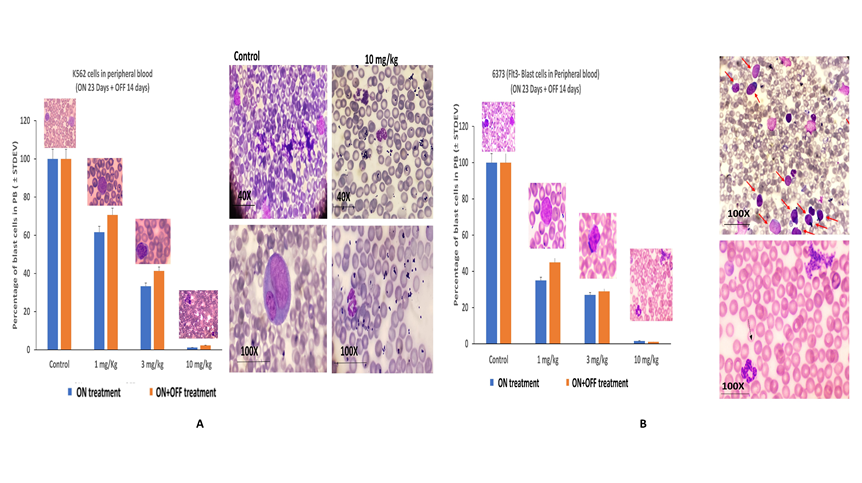
Chart, line chart

Description automatically generated**Supplemental Figure 1. Monitoring of blast cells in peripheral blood in engrafted transgenic mice. A) K562-Luc (AML cell line) in control versus fb-PMT treated mice at different doses over 21 days during treatment and over 14 days post-treatment.** fb-PMT at 1, 3, and 10 mg/kg, subcutaneous daily for 21 days, prevented blast cell expression/reproduction by 35%, 65%, and >95%, respectively, compared to controls. OFF treatment, fb-PMT (10 mg/kg) shows maintained remission. **B) Primary AML cells (6373-FlT3-ITD) cells in peripheral blood in control versus fb-PMT treated mice through 28 days and 14 days post-treatment.** fb-PMT at 1, 3, and 10 mg/kg, subcutaneous daily for 28 days, prevented abnormal blast cell expression/reproduction by 54%, 75%, and 90.5%, respectively, compared to controls. fb-PMT treated mice (10 mg/kg) were in full remission after discontinuation of treatment for 2 weeks, (\*\*\**P*<0.0001, \*\**P*<0.001, \**P*<0.01).

**Supplemental figure 2**



**Supplemental 2. Blood smear from transgenic mice engrafted with leukemic cells. A) K562 cells in peripheral blood (PB) cells, control blood smears versus fb-PMT treated mice at different doses.** Blast cells appeared in the blood smears of NSG-S mice after 10 days. After 21 days of fb-PMT daily subcutaneous injection, the control group showed many blast cells in the peripheral blood, while fb-PMT (1, 3, and 10 mg/kg) treated mice showed a significant decrease in the blast cells by 35%, 65%, and >95%, respectively. The decrease of blast cell percentage in the peripheral blood was dose-dependent. **Left side shows blast cells in peripheral blood in fb-PMT treated animals at different doses ON 21 Days and ON+OFF treatment for 14 days and right side shows representative K562-Luc AML control blood smears versus fb-PMT (10 mg/kg) treated animal cells.** Control group showed immature cells with prominent nucleoli (blast cells) in the peripheral blood. fb-PMT (10 mg/kg) treated animal showed segmented neutrophils with absent blast cells, after 21 days of daily subcutaneous injection. fb-PMT (10 mg/kg) maintained remission after 2 weeks discontinuation. **B) Primary AML cells (6373-FlT3-ITD),** fb-PMT treated at 1, 3, and 10 mg/kg subcutaneous daily for 28 days and 14 days OFF treatment prevented blast cell expression/reproduction by 54%, 75%, and 90.5%, respectively, compared to controls. Right side shows representative image from control group with immature cells and prominent nucleoli (blast cells) in the peripheral blood where fb-PMT (10 mg/kg) treated animal shows segmented neutrophils with absent blast cells. OFF study, 14 days post-treatment, fb-PMT (10 mg/kg) showed successful maintained remission.

Graphical user interface

Description automatically generated**Supplemental Figure 3. IVIS scans of different organs in transgenic mice engrafted with AML K562-Luc and sacrificed after 23 days of fb-PMT (ON treatment).** fb-PMT at 1, 3 and 10 mg fb-PMT treatment, markedly reduced brain, lung, liver, and spleen infiltration with leukemic cells in dose dependent manner (\*\*\**P*<0.0001).

**Supplemental figure 4**

Chart

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**Supplemental Figure 4. Identification and characterization of the 25-gene fb-PMT-induced expression signature in K562 cells.** **A)** Integration into different functional categories of fb-PMT treatment-induced gene expression signatures (GES) as reported in Table 1. **B)** GSEA of 25-gene GES using the TF perturbations followed by expression database. **C)** GSEA of 25-gene GES using the Gene perturbations from gene expression omnibus (GEO) database focused on up-regulated genes. **D)** GSEA of 25-gene GES using the GEO database focused on down-regulated genes. Numbers shown next to the bar graphs report the values of Cumulative scores (Methods).

**Supplemental figure 5**

Chart

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**Supplemental Figure 5. Networks and Ligands associated with the 25-gene fb-PMT-induced expression signature in K562 cells.** **A)** Affected genomic regulatory networks revealed by the GSEA of the Gene perturbations from gene expression omnibus (GEO) database focused on up-regulated (left) and down-regulated (right) genes. **B)** GSEA of the Ligand perturbations from GEO database focused on up-regulated genes. **C)** GSEA of the Ligand perturbations from GEO database focused on down-regulated genes. Numbers shown next to the bar graphs report the values of Cumulative scores (Methods). **D)**  **fb-PMT gene expression signature in K562 cells**

**Supplemental figure 6**

Diagram

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**Supplemental Figure 6. Examples of the specific genes and pathways of potential functional significance revealed by the GSEA of 233 genes down-regulated in KG1a cells after fb-PMT treatment.** **A)** Functionally significant genes down-regulated by fb-PMT treatment in KG1a human AML cells. **B)** GSEA of the TF Perturbations Followed by Expression database (top 30 of 84 significant records). **C)** GSEA of the LINCS L1000 Ligand Perturbations database of up-regulated genes revealed evidence of molecular interference with functions of multiple growth factors in human cancer cell lines. **D)** GSEA of the KEGG 2019 Human database revealed evidence of targeting multiple cancer pathways (including AML).

**Supplemental figure 7**

A picture containing chart

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**Supplemental Figure 7. Identification and characterization of the 39-gene *SNAI* pathway interference expression signature induced by fb-PMT treatment of K562 cells.** **A)** GSEA of the TF perturbations followed by expression database. **B)** GSEA of Ligand perturbations from GEO up-regulation (left) and Ligand perturbations from GEO down-regulation (right) databases. Numbers shown next to the bar graphs report the values of Cumulative scores (Methods).

**Supplemental figure 8**

**Scatter chart

Description automatically generatedSupplemental Figure 8.** **Identification and characterization of the 50-gene fb-PMT signature of molecular interference with estrogen pathway/multi-kinase gene expression regulatory matrix of cell cycle progression.** **A)** 69-gene estrogen pathway interference signature harbors 16-gene estrogen-kinase crosstalk signature. **B)** 50-gene fb-PMT signature of molecular interference with estrogen pathway/multi-kinase gene expression regulatory matrix. **C)** Enrichr pathway analyses of the 50-gene interference signature with estrogen-kinase regulatory matrix identify the cell cycle progression pathway as the principal target. **D)** GSEA of the 50-gene interference signature with estrogen-kinase regulatory matrix using the DisGeNET database of human disorders.