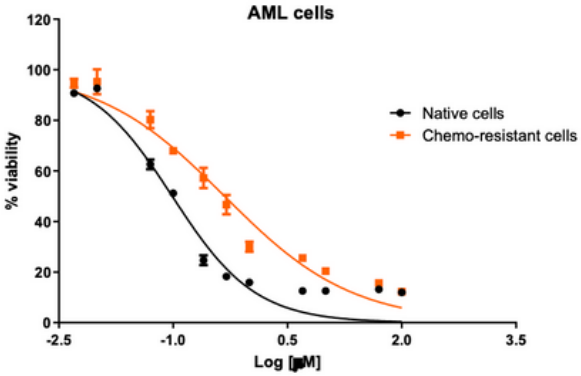
Overcoming Chemotherapy Resistance in Cancer, a Tailor-made model development

Overview: Chemotherapy resistance remains a major challenge in treating aggressive cancers such as Acute Myeloid Leukemia (AML), Small Cell Lung Cancer (SCLC), and triple-negative breast cancer. Our client sought to evaluate a novel compound targeting resistance mechanisms.

Goal: To develop a custom tumor model resistant to standard chemotherapy and assess whether the compound (re)sensitize tumors and improve treatment outcomes.

Our Approach:

In Vitro – Generation of Cytarabine-Resistant Cell Line



We generated AML cells resistant to cytarabine, showing a stable 3- to 4-fold resistance even after freeze-thaw cycles. This robust model provided a reliable platform for downstream *in vitro* and *in vivo* efficacy testing.

In Vitro efficacy

Test Compound	IC_{50} (µM)	Fold Resistance vs. Native Cells
Native Cells	0.09	—
Resistant Cells (untreated)	0.33	x3.7
Vehicle	0.31	x3.4
Client Test Compound	0.11	x1.2
Negative Control compound	0.34	x3.8

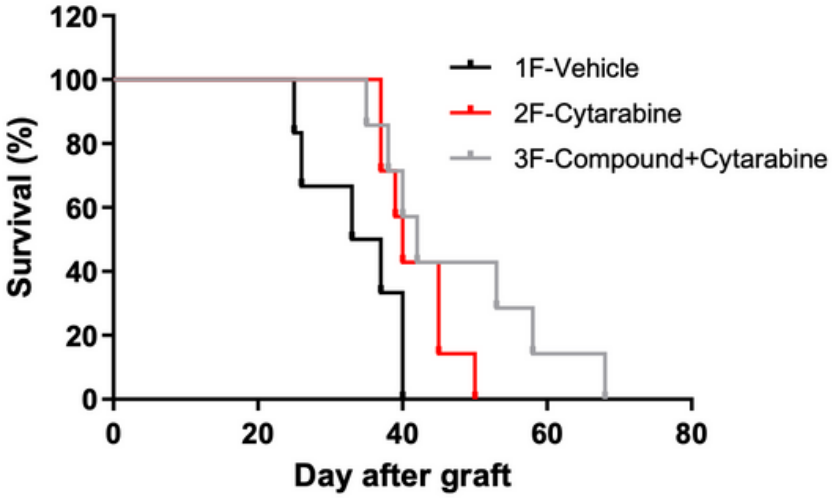
Treatment with the client's test compound significantly decreased the IC_{50} of cytarabine-resistant cells to 0.11 µM, effectively re-sensitizing them to levels close to those of native non-resistant cells.

This result highlights the compound's potential to overcome cytarabine resistance, providing compelling evidence for its mechanism of action. The vehicle and negative control compound had no impact on resistance with IC_{50} values remaining elevated (0.31–0.34 µM, ~3.4–3.8-fold higher than native cells), confirming that the observed re-sensitization was specific to the client's test compound.

In Vivo efficacy

To meet our client's specific needs, we set up an orthotopic AML model using intravenous injection of cytarabine-resistant cells in immunodeficient mice. This model mimics aggressive, disseminated disease and is ideal for evaluating re-sensitizing therapies.

Model Validation Results



Cytarabine alone increased mean survival from 34 to 42 days, yielding a 23.5% increase in lifespan (ILS) – though not statistically significant. Cytarabine + compound extended survival to 48 days, corresponding to a 41% ILS, with statistical significance ($p < 0.05$).

Conclusion

This tailor-made studies confirmed that the client's compound re-sensitizes cytarabine-resistant AML, restoring drug response *in vitro* and improving survival *in vivo*. These results highlight its potential to overcome resistance and support further investigation.

Why Work With Dev4All?

At Dev4All, we specialize in designing tailor-made preclinical models that align with your scientific and strategic goals. Whether you're targeting drug resistance, exploring novel mechanisms, or optimizing combination therapies, our strength lies in understanding your needs and building the right model to meet them.
We help your oncology programs move forward by:

- Translating complex questions into actionable, customized in vivo models
- Supporting proof-of-concept studies with robust and relevant data
- Streamlining lead candidate selection with agile and high-quality experimentation
- Adapting quickly to evolving research priorities and therapeutic strategies

Let's collaborate!

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