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Zebrafish Models

Acute Myeloid Leukemia (AML)

Phenotype, Biomarkers

3 Great Questions in Leukemia Discovery

Dr.Bibhas Kar

Common Oncology Drugs & Zebrafish Mechanisms

Imatinib, Venetoclax, Daratumumab

PENTAGRIT
Zebrafish
CRO

About Us

Pentagrit CRO specializes in zebrafish models for hematological malignancies, offering ready-to-screen assays for lead identification, mechanism of action studies, and toxicity profiling.

From real-time in vivo imaging to high-throughput therapeutic screening, our zebrafish models accelerate insights into hematological malignancies like AML, CML, and Multiple Myeloma—bridging discovery to delivery.

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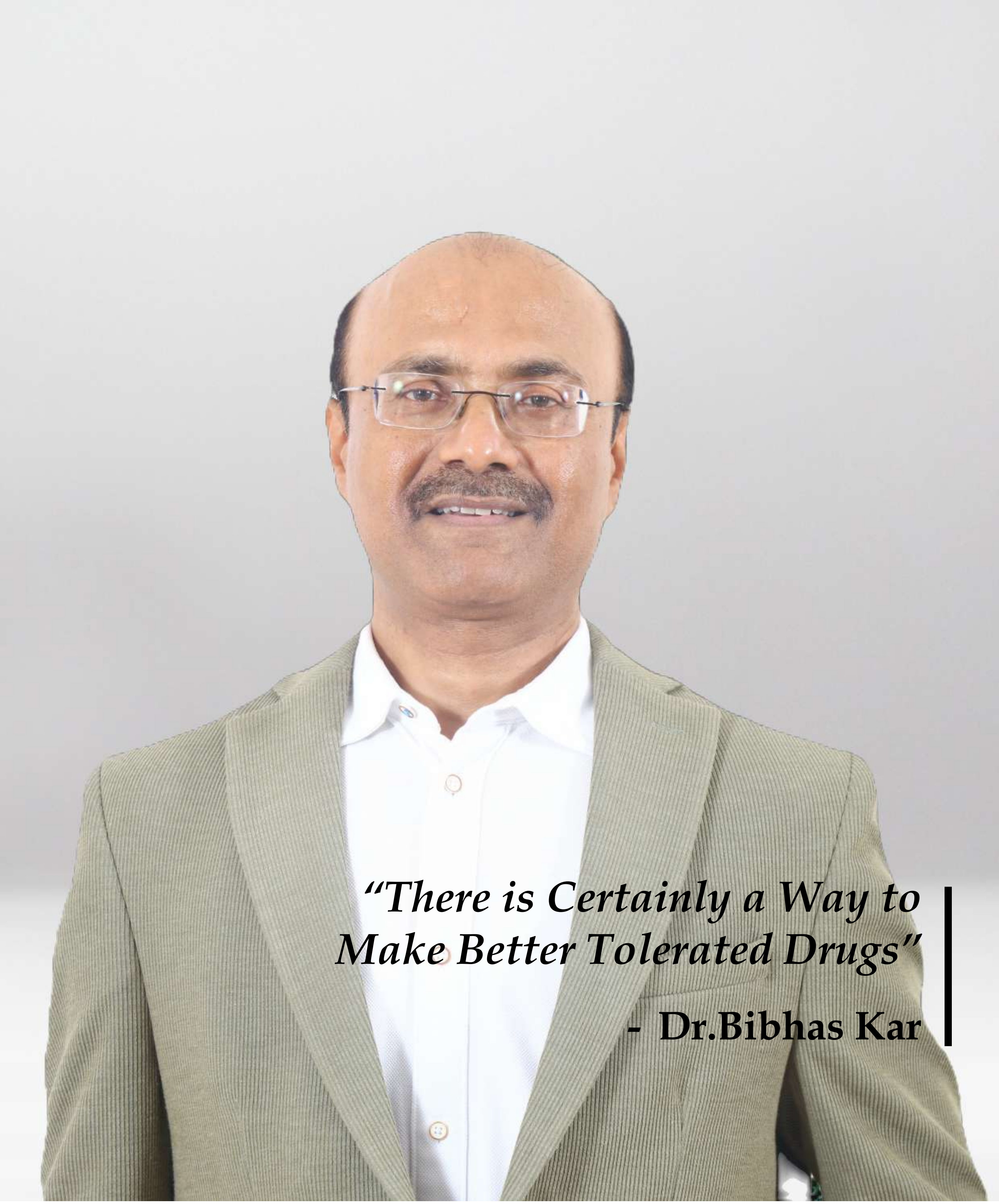
Common Oncology Drugs & Zebrafish Mechanisms

1. Imatinib
2. Venetoclax
3. Daratumumab

Featured Scientist:



3 Great Questions in Leukemia Drug Discovery

What can drug discovery do

Q. A

To help drug intolerance in patients?

During drug discovery process, the dose effect is measured for a population. Ultimately, we are prescribing population data to individual patients, Personalized drug therapy is still far away. However, with the advent of AI, we can link markers of patients who would show adverse effects. For example, EGFR mutations are linked to tyrosine kinase inhibitors (TKI) adverse effects. Similarly, additional markers for intolerance should be identified. This can help classify the patient before going in for a specific therapy. Currently the markers of drug intolerance are not specific. They are such as skin rashes, indigestion, vomiting etc. What I am saying is that - at the drug discovery level, we need to identify the 2% or so animals that are drug intolerant unlike the rest of the animals and evaluate them for which physiological function and genotype they (remove they) are different from other animals.

Q. To manage drug resistance?

A. This I feel has more to do with the sporadic nature of the tumor. It's hard to say how each tumor behaves in individual physiological system. In my opinion, a drug for a drug could be a great idea. For example, can we target resistance by interfering with pathways through which tumor becomes resistance. It is a well known fact that signalling pathways have a huge role in tumor resistance. Can drugs that interfere with tumor signalling for resistance be evaluated? The other proposal, is can we constantly change the nature of treatment, say as the patient reaches the peak of response stage and waiting until the tumor evolves. Can we change the nature of treatment by term of the disease and progress of the patient. This prevents the natural selection process of tumor to one specific mechanism of drug resistance.

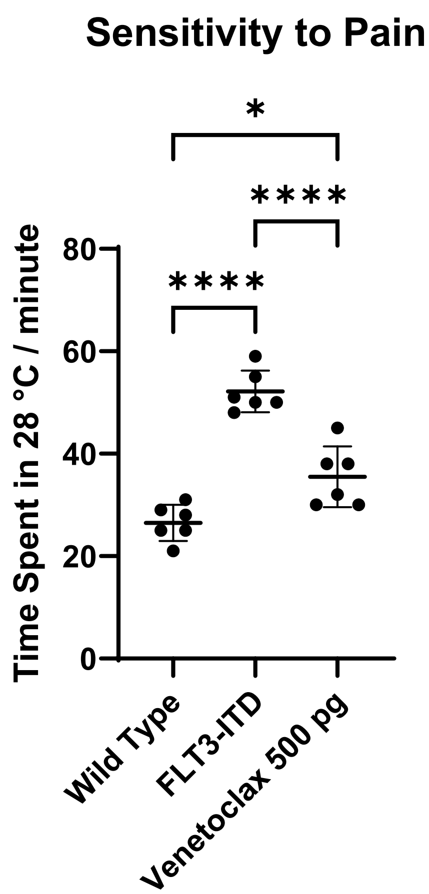
Q. To improve quality of life?

A. Quality of life studies I feel are much more than social, diet and exercise. I feel it also has to do with the hormones of the patient. We need to identify what factors drive pathological hormones such as cortisol and insulin high. Are they also related to drug intake. If so, then this question needs to be addressed at the beginning of the drug discovery. Toxicity of the drug should also be measured beyond pathology but also into deeper behavioral aspects. For example, serotonin levels, sleep wake cycles and circadian balance. Digestion parameters such as leptin and ghrelin, could be verified as well during drug screening process.

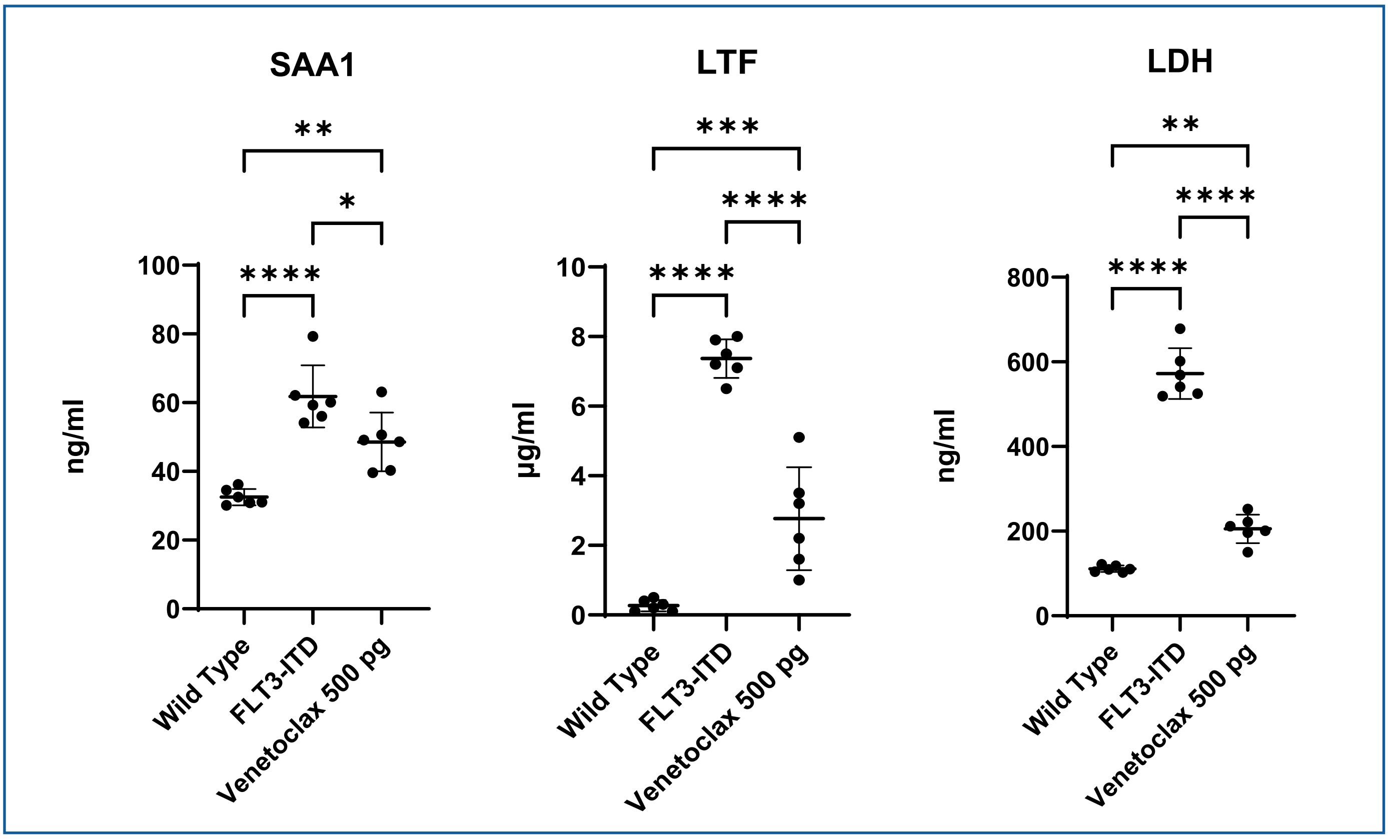
Acute Myeloid Leukemia (AML)

Phenotype: Pain and Anaemia

Our zebrafish models of AML recapitulate key pathological hallmarks, including the expansion of immature myeloid progenitors and failure of differentiation. A key biomarker is the ***FLT3-ITD mutation***, which drives leukemic proliferation through constitutive activation of the FLT3 receptor. Additional plasma biomarkers such as Serum Amyloid A1 **(SAA1)**, Lactate Dehydrogenase **(LDH)**, and Lactotransferrin **(LTF)** are monitored to assess systemic inflammation, tissue damage, and iron-binding activity associated with leukemic progression.



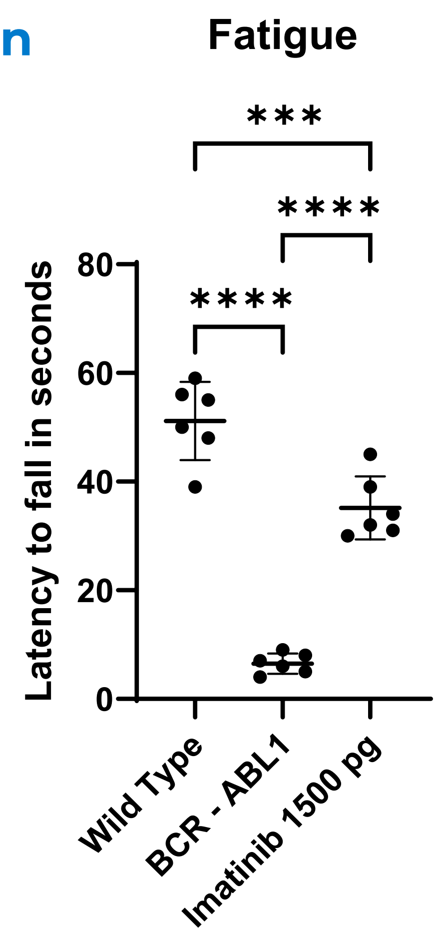
Biomarkers: Plasma - Serum amyloid A1, Lactotransferrin (LTF) and Lactate Dehydrogenase (LDH)



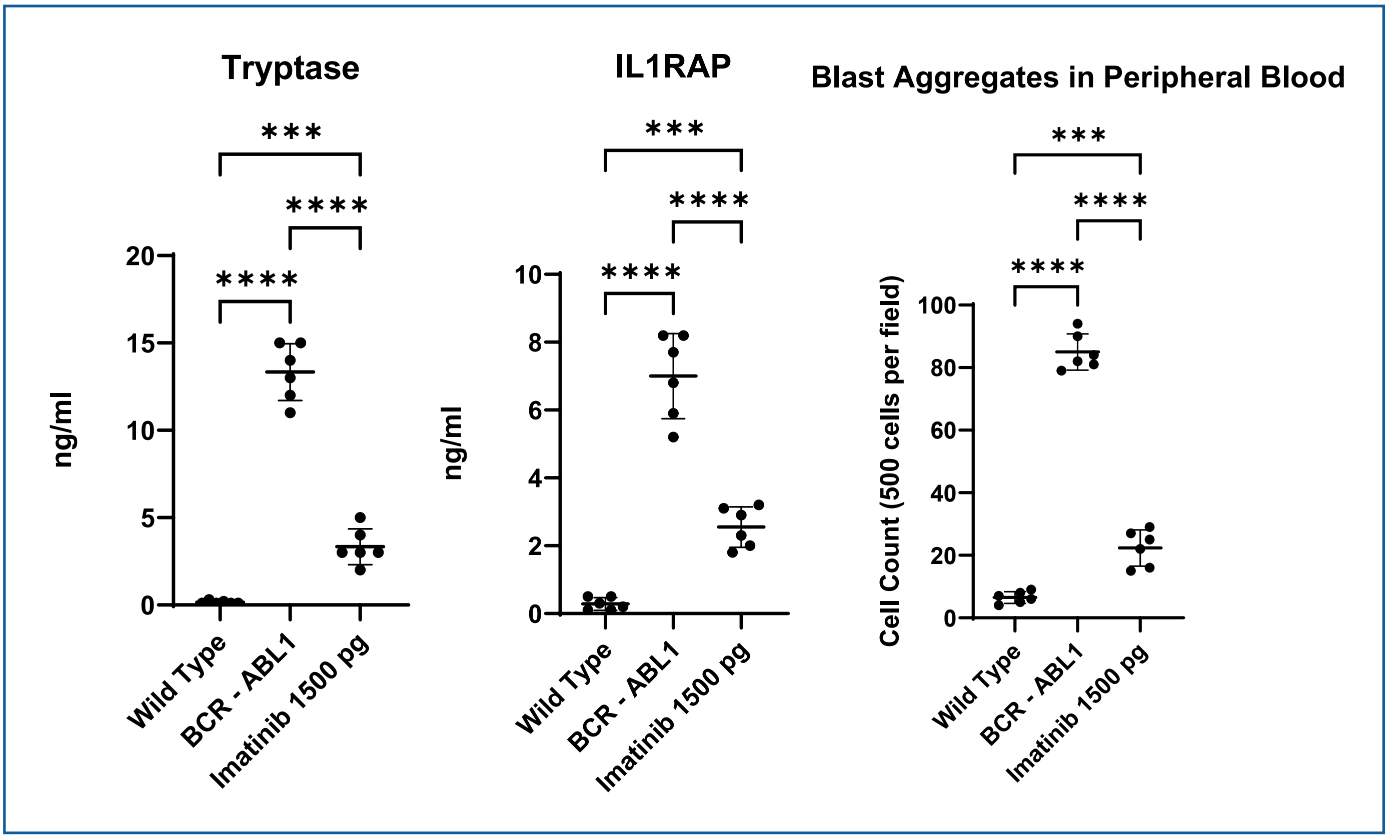
Chronic Myeloid Leukemia (CML)

Phenotype: Fatigue and Enlarged spleen

The zebrafish model of CML mimics the human disease by expressing the ***BCR-ABL fusion gene***, a constitutively active tyrosine kinase that disrupts normal hematopoiesis and enhances the survival of leukemic progenitors. Serum biomarkers such as **Tryptase**, Interleukin-1 Receptor Accessory Protein **(IL1RAP)**, and the presence of **blast aggregates in peripheral blood** are evaluated as indicators of disease burden, mast cell activation, and leukemic cell circulation.



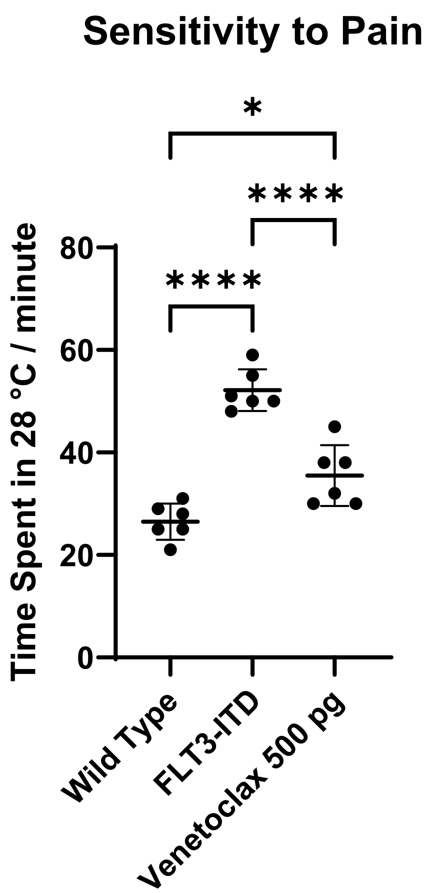
Biomarkers: Serum -Tryptase, IL1RAP and Blast Aggregates in Peripheral Blood



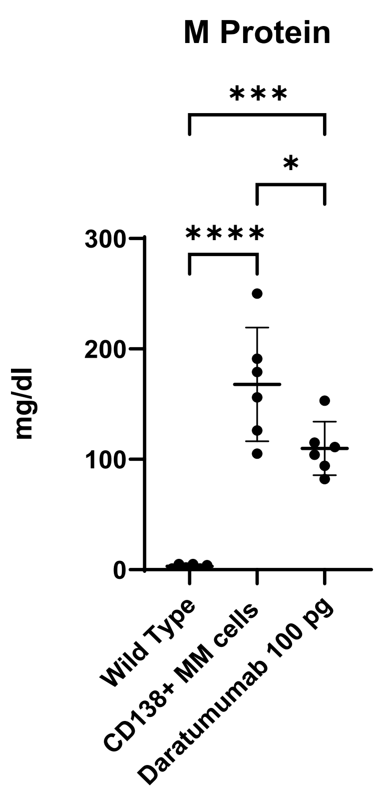
Multiple Myeloma (MM)

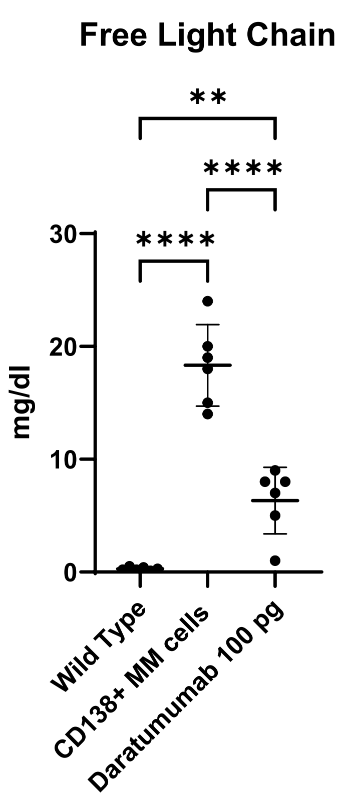
Bone Lesions & Hypercalcemia in Serum

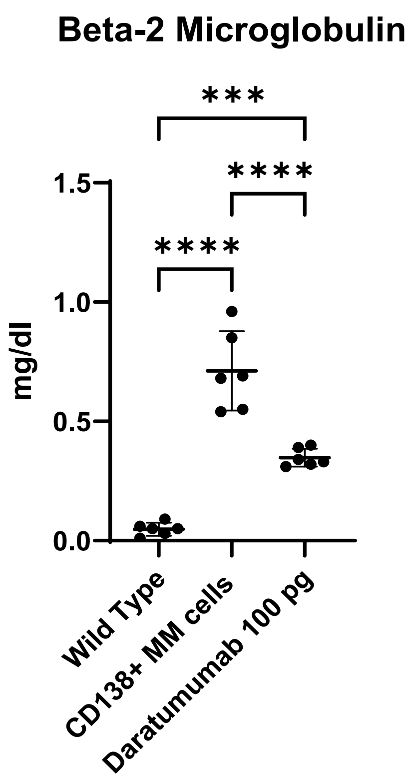
Zebrafish models of multiple myeloma (MM) allow real-time tracking of malignant plasma cell growth and interaction with the bone marrow–like environment. ***CD138***, a key plasma cell marker, is visualized using fluorescently labeled human MM cells. Serum biomarkers such as **M-protein**, a monoclonal immunoglobulin produced by myeloma cells; Free Light Chains **(FLCs)**, indicating abnormal antibody secretion; and Beta-2 Microglobulin **(β 2M),** a marker of tumor burden and disease severity, are evaluated to monitor progression and therapeutic response.



Biomarkers: Serum - M-protein, Free Light Chain and Beta-2 Microglobulin







In Vivo Drug Mechanism Profiling in Zebrafish Models of Leukemia and Myeloma

In our zebrafish models, several commonly used or repurposed drugs for hematological malignancies demonstrate clear mechanisms of action and measurable in vivo responses. **Imatinib**, used in Chronic Myeloid Leukemia **(CML)**, effectively inhibits the proliferation of BCR-ABL+ cells and helps restore normal hematopoiesis. **Venetoclax**, used in both Acute Myeloid Leukemia **(AML)** and Multiple Myeloma **(MM)**, induces apoptosis through **BCL-2 inhibition**, with cell death quantified via TUNEL staining in zebrafish embryos.

For Multiple Myeloma **(MM)**, **Daratumumab** is a monoclonal antibody that targets CD38 on malignant plasma cells and induces their clearance through immune-mediated mechanisms. In zebrafish models, human MM cells expressing **CD38** and **CD138** are injected and tracked using fluorescent markers. Upon treatment, Daratumumab significantly reduces the burden of these labeled plasma cells. This reduction is visualized in real-time, enabling dynamic assessment of drug response.

Sandhiya S

Looking to accelerate your Oncology pipeline with zebrafish models?

Our team supports CRO collaborations from early discovery to IND-enabling studies. Let's discuss your screening needs.

sandhiya@pentagrit.com