CROWN BIOSCIENCE

HuKemia®

A unique collection of patient-derived blood cancer models

A JSR Life Sciences Company

FACTSHEET

V1.0

The HuKemia® Blood Cancer PDX Collection

Evaluate blood cancer therapeutic candidates with Crown Bioscience's validated, stable, truly patient representative leukemia models.

HuKemia®

HuKemia is Crown Bioscience's collection of validated blood cancer PDX models, fully annotated with patient information, diagnosis, and clinical treatments. These models have been fully quality controlled by our pathologists and are available with genotyping and phenotyping data.

What are Blood Cancer PDX Models?

In drug discovery, animal models are used to understand the efficacy, PD, PK, metabolism, and tolerability of candidate drugs. In oncology, these have traditionally been cell line derived xenograft (CDX) models utilizing cell lines which have been immortalized *in vitro* from patient tissues.

PDX models are generated directly from patient samples, which are implanted into mice without *in vitro* propagation. For our blood cancer PDX models, peripheral blood or bone marrow is taken from patients, and implanted directly into mice to generate the original model, which can then be utilized to evaluate lead compounds for a variety of pharmacological properties (PD, efficacy, etc.), as well as disease indication and demographic specificity.

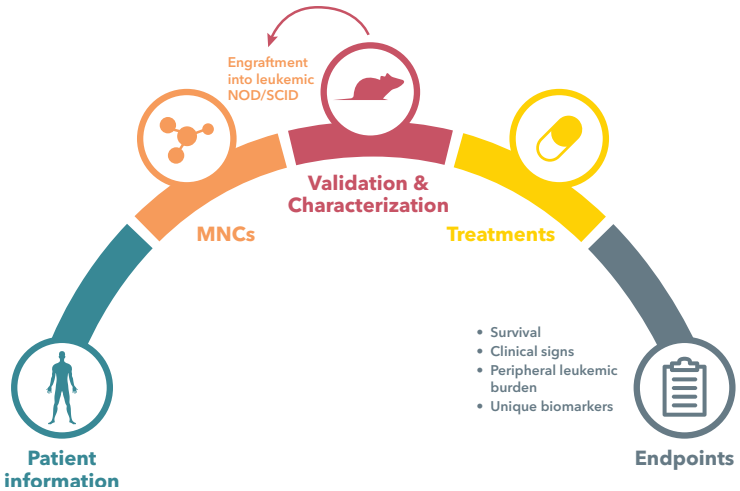
As PDX models closely reflect patient tumor histo- and molecular pathology they offer a highly predictive model for preclinical drug evaluation.

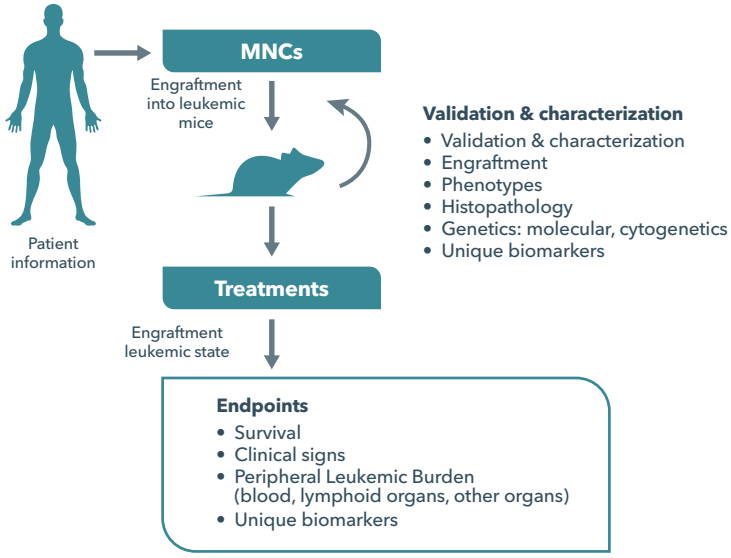
Advantages of the HuKemia Blood Cancer PDX Collection

Crown Bioscience's validated and well-characterized HuKemia models provide many advantages:

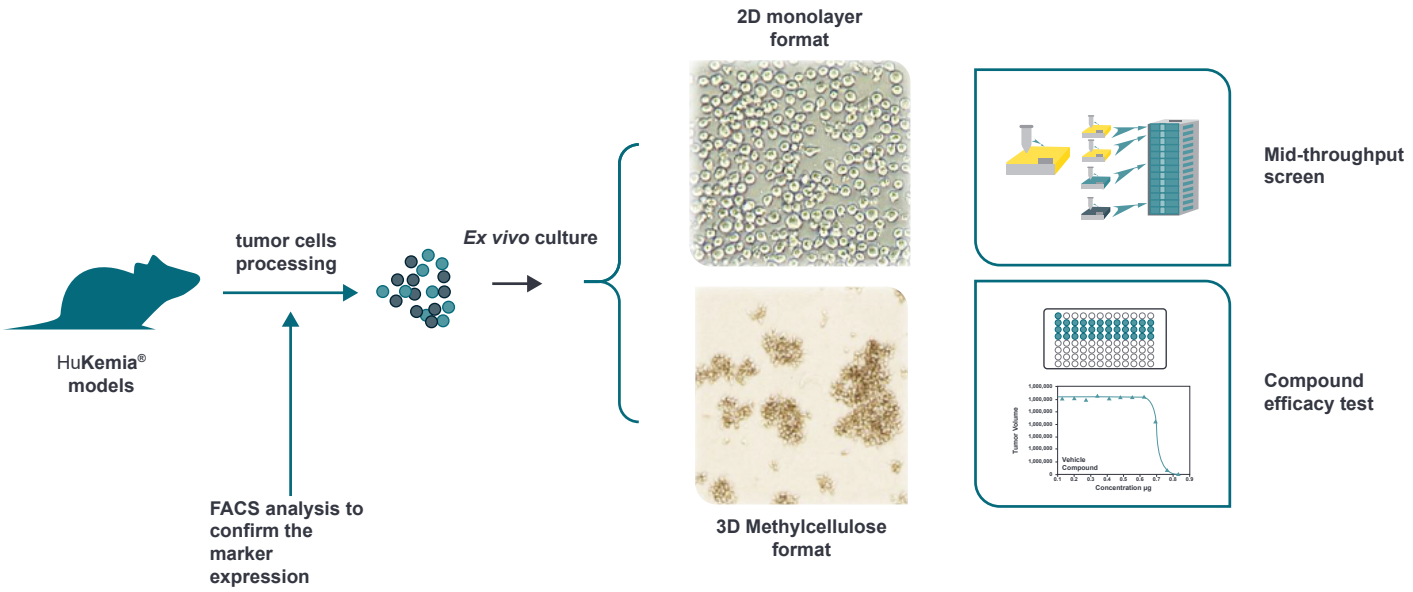
- Well-established models that have been used in over 100 preclinical studies, and are therefore a tried and tested approach for assessing preclinical efficacy
- Derived from patients treated with today's clinical therapeutics, including SOC targeted therapies and immunotherapeutics
- Present as stable disease that is transferable through passages, meaning results are highly reproducible across studies
- Overcome limitations with CDX models for systemic diseases. When utilizing CDX models, it can be highly challenging to detect the leukemic cells in the blood, limiting studies to only monitoring survival
- Can be repeatedly challenged to mimic clinical therapy and the emergence of resistance, which means that models of resistance can be created for testing next-generation drugs
- Optional *ex vivo* assays to leverage access to fresh tumor samples for all AML and ALL models, enabling the assessment of efficient combination and dosing regimens. An illustration of the HuKemia study design followed by *ex vivo* workflow is shown below

HuKemia Study Design





Ex vivo workflow



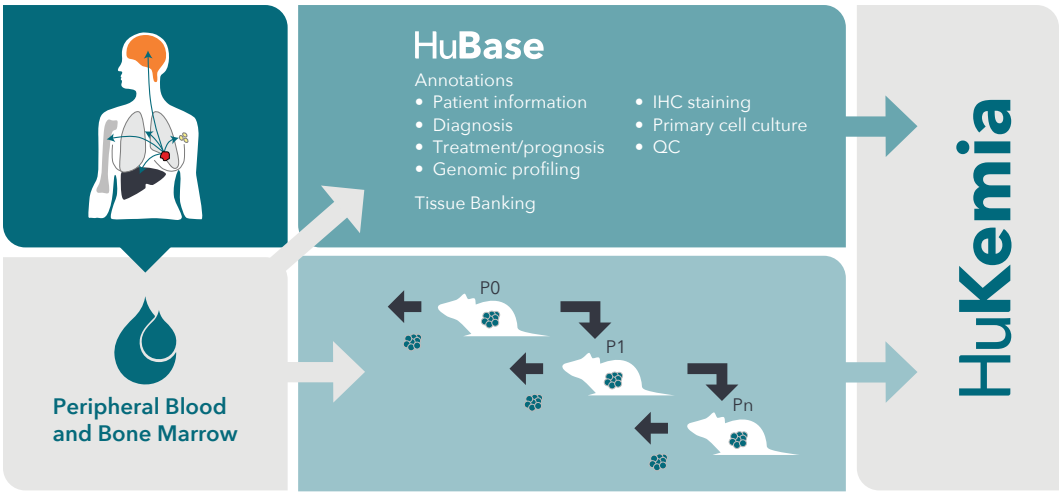
The HuKemia collection is made up of:

- 17 Acute Lymphoblastic Leukemia models
- 10 Acute Myeloid Leukemia models

Characteristics of the HuKemia Blood Cancer PDX Collection

- Patient-relevant mutations e.g. IDH2 mutation, FLT3-ITD(+), BCR/ABL(+)
- Unique models for targeted therapy
- Well-characterized for pathology, growth characteristics, and response to standard of care (SoC) agents
- Genetically/genomically annotated for gene expression, gene copy number, mutations, and fusions via NGS technologies
- Online, searchable database (HuBase™) of phenotypic and genotypic data, patient information, growth curves, and SoC treatment data

HuKemia Blood Cancer PDX Collection



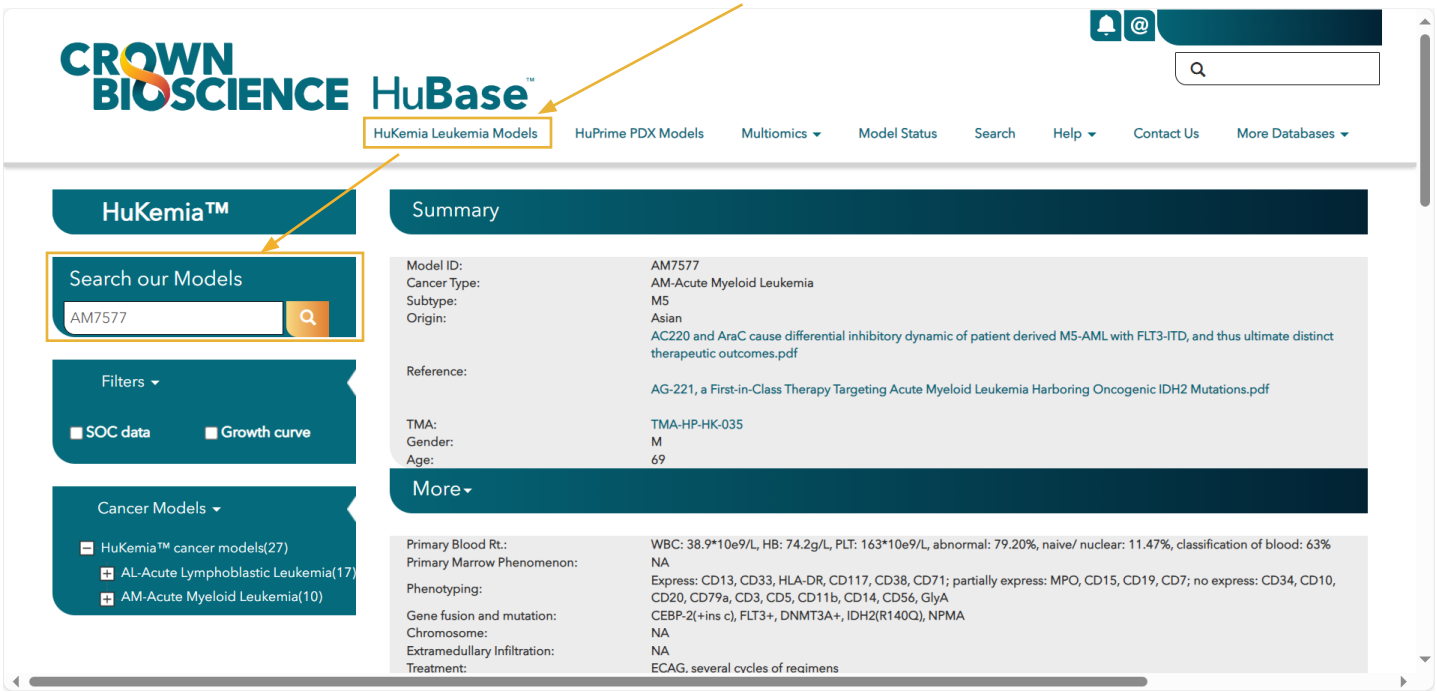
Newly Updated Acute Myeloid Leukemia Model Collection

Model ID	Patient Information			
	Cancer Type	Stage	Gene Mutation	Treatment History
AM9626	Acute myeloid leukemia	Unavailable	FLT3-D835H; NPM1-W288Cfs*12; DNMT3A-R882H; IDH1-R132H	Allogeneic HSCT | Sorafenib | Hydroxyurea | Decitabine
AM9627	Acute myeloid leukemia	M7	KMT2C-C391*	Unavailable
AM9628	Acute myeloid leukemia	M5a	FLT3-N676T; KMT2C-C391*; t(9;11)(p22;q23); MLL-AF9	Untreated
AM9624	Acute myeloid leukemia	Unavailable	FLT3-D835Y; RAD21-R586*; RUNX1-S265Efs*335; WT1-R380Gfs*3; WT1-R369Afs*16	Cytarabine | Cytarabine + Idarubicin | RIC HSCT
AM7125	Acute myeloid leukemia	M4	AML1/ETO-, CBFb/MYH11-, WT1/ABL= 117%, FLT3-ITD+, NPM1 mutation+	Chemotherapy
AM7407	Acute myeloid leukemia	M4	Unavailable	Intravenous nutrition, assisted ventilation with respirator. antibiotics therapy, IA chemotherapy
AM8231	Acute myeloid leukemia	M2	No gene fusion; FLT3-ITD+(weak);NPM1/ALB=73.91%	Unavailable
AM5512	Acute myeloid leukemia	Unavailable	Unavailable	Unavailable
AM7577	Acute myeloid leukemia	M5	CEBP-2(+ins c) FLT3-ITD DNMT3A+ IDH2(R140Q) NPMA	ECAG, several cycles of regimens
AM8096	Acute myeloid leukemia	M2	Unavailable	Unavailable

The full suite of patient and technology platform annotations can include:

- U219 gene chip array analysis (mRNA)
- SNP6.0 array analysis
- miRNA profiling
- Whole exome sequencing (WES)
- Transcriptome sequencing
- Short Tandem Repeat (STR) genotyping
- Phenotyping, including HLA test
- Primary blood test results
- Primary marrow morphology
- Patient & model treatment and post treatment
- Gene fusion and mutation
- Growth curves
- SoC response curves

For complete characterization data, including phenotypic and genotypic data, patient information, growth curves, and SoC treatment data, login to Hu**Base™** our online, searchable database.



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