

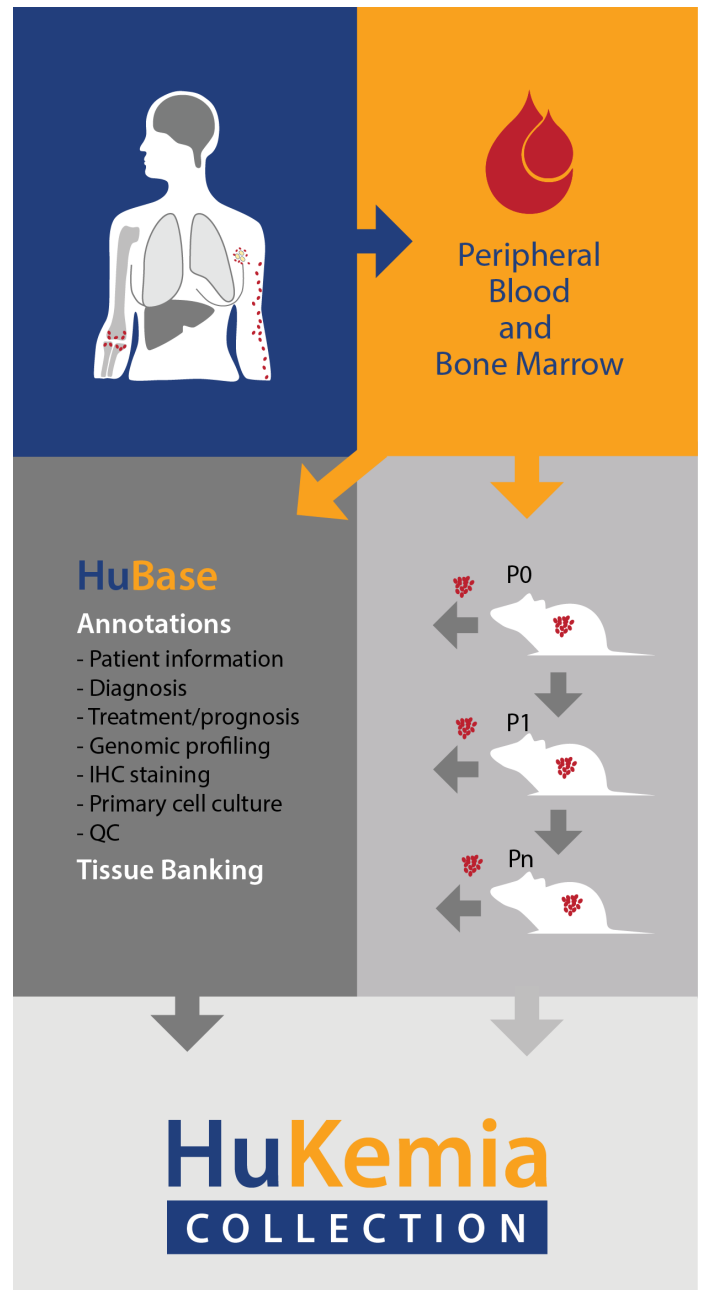
In vivo and *ex vivo* ALL and AML patient-derived blood cancer models for efficacy testing

Discover the benefits of using **HuKemia** the only validated, stable, truly patient representative leukemia models commercially available, to accelerate your agent efficacy evaluation and blood cancer drug discovery programs.

Today, over 95% of oncology clinical trials fail, with 50% of these due to lack of efficacy in the clinic. Using patient-derived xenograft (PDX) oncology models including blood cancers, is the most accurate approach to predicting clinical efficacy, before entering the clinic.

CrownBio's validated and fully characterized **HuKemia** models are commercially unique, in that they:

- Present as stable disease transferable through passages, which means that results are highly reproducible across studies.
- Are the only commercially available PDX blood cancer models that truly represent the human disease, meaning they provide a unique stable resource for studying disease mechanisms and the efficacy of therapeutics.
- 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.
- Are established models that have already been used in over 100 preclinical studies, and are therefore a tried and tested approach for preclinical efficacy screening.





HuKemia Key Facts

HuKemia Characteristics

- The **HuKemia** collection is made up of:
 - › 19 Acute Lymphoblastic Leukemia
 - › 6 Acute Myeloid Leukemia models.
- Stable models with typical leukemia symptoms and eventual mortality, truly representative of the human condition.
- 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.
- Curated, online, searchable database (**HuBase™**) of phenotypic and genotypic data, patient information, growth curves, and SoC treatment 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 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 solid tumors, this means implanting patient tumor tissue, and subject to this “taking” in the host and reasonable growth rates being achieved, the tumor tissue can be subsequently passaged on into further animals and become a PDX model.

For blood cancer PDX models peripheral blood or bone marrow is taken from patients, and implanted 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.

Why choose PDX rather than Cell Line Derived Xenografts?

All models have their place in the drug discovery process. Cell line derived xenografts are easy and widely used tools for the initial evaluation of multiple potential candidates or a compound series, to evaluate and rank efficacy against a known target which a particular cell line may be known to express.

For systemic disease however, cell line derived xenograft models have limitations – it can be highly challenging to detect the leukemic cells in the blood, limiting studies to only monitoring survival. Our validated, stable PDX models allow efficacy studies in models truly representative of the human condition.

HuKemia

HuKemia is CrownBio's collection of blood cancer PDX models, which have been QC'd to determine whether they are “fit for efficacy” studies. They are validated models, fully annotated with patient information, diagnosis, and treatments, which have been fully quality controlled by our pathologists, and are genetic fingerprinted.

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

HuKemia Models are Commercially Unique

Most commercially available blood cancer PDX models are transient in nature, and non-transferable through passages (not renewable), without disease symptoms or mortality. While they can provide a gross measure of response, they have a finite banked leukemia source from patients, only allowing a one-shot study.

HuKemia models including ALL and AML PDX however, are unique.

1. Show typical leukemia symptoms and eventual mortality
2. Truly representative of the human condition
3. Primary and relapsed disease
4. Validated stable models

As our HuKemia models are permanent, they allow the study of disease recurrence after initial treatment challenge and the efficacy testing of novel agents against drug resistance.

A Variety of Subtypes and Phenotypes Available

Our two most highly characterized models (AM7577 and AM8096) include different subtypes and phenotypes, and our full collection provides further subtypes, fusions, and mutations of interest.

Model AM7577

An M5 subtype model, which has a more differentiated phenotype with the leukemic cells traveling beyond the marrow into the periphery. The model has an IDH2 mutation and is the only commercially available validated, stable PDX model of this type, it is also FLT3-ITD+.

Model AM8096

An M2 subtype model with a less differentiated phenotype with leukemic cells mostly limited to the bone marrow.

CrownBio HuKemia AML Models Genetic Characterization

Model ID	Subtype	Gene Fusion and Mutation	Ready for Service?
AM5512	M7 (TBC)	TBC	Yes
AM7076	M2 (R3: 86.3%)	AML1/ETO(-), BCR/ABL(-), MLL(-), FLT3-ITD(+), NPM1(-)	Currently undergoing validation
AM7247	M1 (R3: 87.5%)	AML1/ETO(-), CBFb/MYH11(-), FLT3-ITD(+), WT1/ABL=121%, NPM1 mutation(+), medullary system related gene all(-), MLL related gene(-)	Currently undergoing validation
AM7440	CML-M5	AF10, BCR/ABL(+), BCR/ABL 62.1%.	Currently undergoing validation
AM7577	M5	IDH2(R140Q), FLT3-ITD(+), DNMT3A R882H, NPM1 and CEBPA insertion (SNP)	Yes
AM8096	M2	WT: TP53, FLT3, NPM1 CEBPA-exon1: insertion 570-587, 3GCACCC>4GCACCC	Yes



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Explore Scientific Data

Log into [HuBase](#) to review PDX model data.
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