Cancer and Blood Disease Institute

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CBDI

The Cincinnati Children's **Cancer and Blood Diseases Institute** (CBDI) is one of the largest clinical care and research centers for pediatric cancers and blood diseases in the United States. The CBDI offers…

- Advanced patient therapeutics, providing innovative treatment of rare, relapsed and recurrent cancers
- Physicians specialized in specific cancers providing expertise and resources to treat the most challenging conditions.
- Cutting edge research to improve the outcome for cancer patients around the world
- Top 3 in the nation pediatric cancer care for children and adolescents, as voted by U.S. News 2012

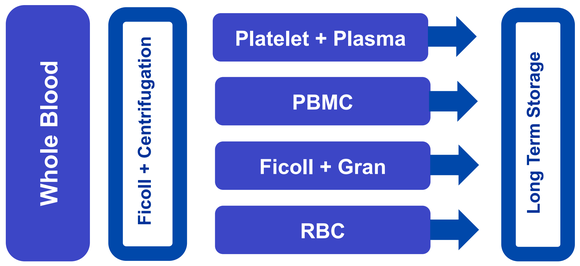
CCSS

The **Children's Cancer Survivor Study** (CCSS) is a longitudinal cohort study for the long-term follow-up of survivors of childhood cancer.

The age dependent increase in cardiovascular mortality seen in the normal population may occur both earlier and be more severe in childhood cancer survivors. The frequency of such events is likely to be influenced by both prior therapy and genetic background. The database provides the opportunity to study these contributory factors in a well defined population.

The Davies laboratory supports the CCSS through sample collection and processing

Blood and Marrow Processing



Using a Ficoll gradient and centrifugation, whole blood drawn from a patient can be separated out into its constituent parts (platelets + plasma, peripheral blood mononuclear cells (PBMCs), granulocytes and red blood cells). These can then be stored appropriately for future testing.

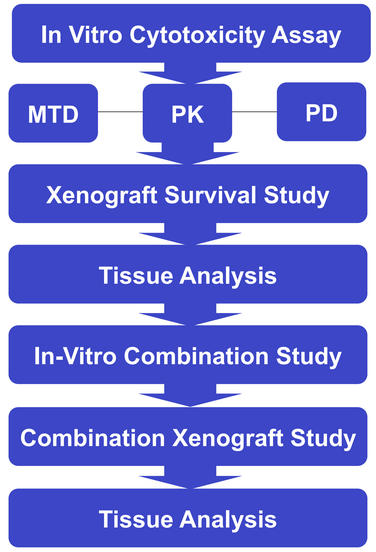
From Bench Top to Clinic

Novel Therapeutic Development Timeline

Process	Time (Years)	# of Compounds
Drug Discovery	3-6	5000 – 10,000
Pre-Clinical Studies		250
Clinical Studies Phase I-III	6-7	5
NDA Reviewing Applications	0.5-2	1
Post Approval Studies		1
Final Approval		1
Clinic		1

From initial discovery to final clinical use, drug development takes years of research and billions of dollars of investment.

Pre-Clinical Testing of Novel Cancer Therapeutics



In vitro (cell line) and in vivo (animal) testing is carried out to test the efficacy and specificity of candidate compounds.

This provides valuable information on how the drug works (mode of action) and its safety profile (dose level/ route/ regimen).

Drug combination studies can also be run to determine potential positive and negative drug interactions prior to subsequent clinical testing.

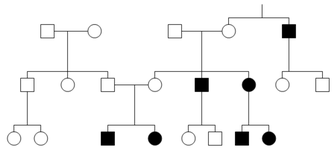
From Clinic to Bench Top

The Tissue Repository

The Tissue Repository is a research study geared towards Solid Tumors/ Leukemia-Lymphoma and Vascular Malformations. The purpose of the study is to collect bone marrow, peripheral blood, buccal cells, spinal fluid, urine, and or involved tissue samples. Demographic information, past medical history, and clinical test results are also collected to create a longitudinal research database of patients.

A long term storage facility houses the samples and medical information. In some instances, family members may also be asked to provide samples and information. By conducting these studies, researchers hope to learn more about, and come up with better, treatments for tumors and possibly other diseases as well. These studies can include work to…

1) identify changes in genes and proteins,
2) identify genes involved in drug metabolism and response
3) test new treatments against tumors.



Personalized Medicine

In 2003 sequencing of the first human genome was completed. This massive accomplishment took an international effort of 13 years at a cost of $3 billion. Today this same task can be completed for ~$1000 on a single bench top in just a few hours. The incredible rate of advancement in sequencing technology brings personalized medicine, based on an individuals genetic data closer than ever to standard clinical practice.

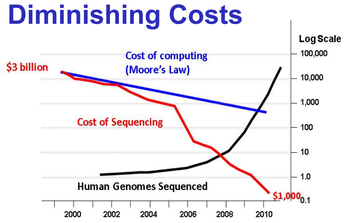
The Ion AmpliSeq™ Cancer Panel targets 50 genes

ABL1	EZH2	JAK3	PTEN
AKT1	FBXW7	IDH2	PTPN11
ALK	FGFR1	KDR	RB1
APC	FGFR2	KIT	RET
ATM	FGFR3	KRAS	SMAD4
BRAF	FLT3	MET	SMARCB1
CDH1	GNA11	MLH1	SMO
CDKN2A	GNAS	MPL	SRC
CSF1R	GNAQ	NOTCH1	STK11
CTNNB1	HNF1A	NPM1	TP53
EGFR	HRAS	NRAS	VHL
ERBB2	IDH1	PDGFRA	
ERBB4	JAK2	PIK3CA	

Advantages of Personalized Medicine

- More precise diagnoses
- Greater predictability of disease progression
- Greater understanding of disease etiology
- Improved patient safety
- Right drug for the right patient
- Right drug dose for the right patient

Diminishing Costs



Sequencing Workflow