NCI Division of Cancer Biology

Human Cancer Models Initiative (HCMI):

A Community Resource of Next-generation Cancer Models

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NIH NATIONAL CANCER INSTITUTE

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There is a need for improved cancer models

- Traditional cell lines lack ***associated clinical data***, matched ***normal tissue***, and do not recapitulate the ***microenvironment*** of cancer
- Results in animal models do not always lead to ***breakthroughs in human studies***
- It is unethical or impossible to perform many experiments in humans

The Human Cancer Models Initiative (HCMI)

- HCMI is an international consortium founded by ***NCI***, ***Cancer Research UK***, ***Wellcome Sanger Institute***, and the foundation ***Hubrecht Organoid Technology***
- Over ***800 patient-derived Next-Generation Cancer Models (NGCMs)*** have been generated
- Models have been generated from many cancer types, including rare and pediatric cancers
- ***337 models*** are available to the research community at ATCC, with more on the way

Outline (1)

- How are models generated and quality controlled?
- What models are available?
- HCMI webpages & resources

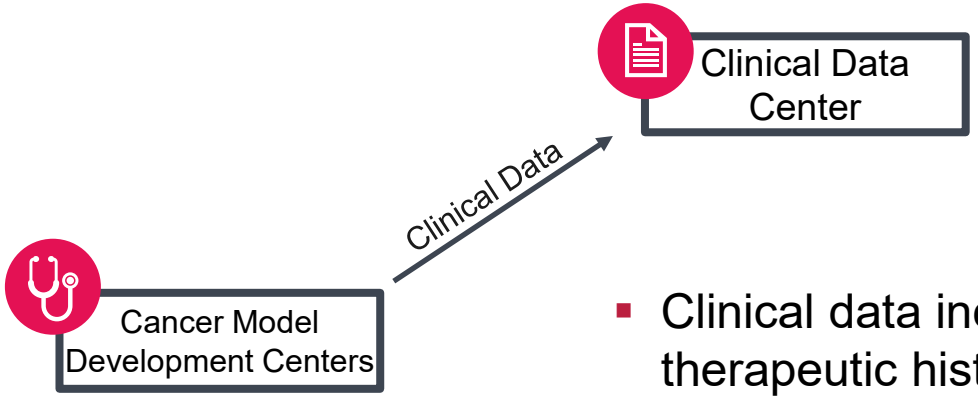
Outline (2)

- **How are models generated and quality controlled?**
- What models are available?
- HCMI webpages & resources

Cancer Model Development Centers (CMDCs) generate models

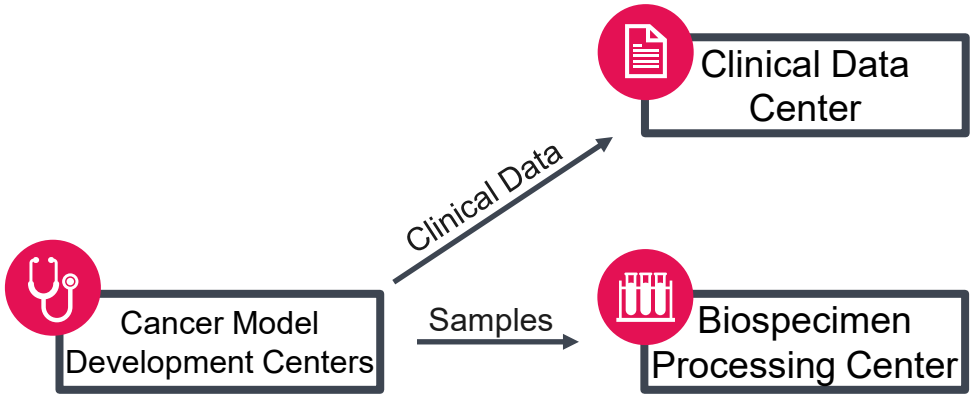
- CMDCs include the Broad Institute, Cold Spring Harbor Laboratory, Stanford University, and Weill Cornell Medical College

The Clinical Data Center (CDC) harmonizes & quality controls clinical data

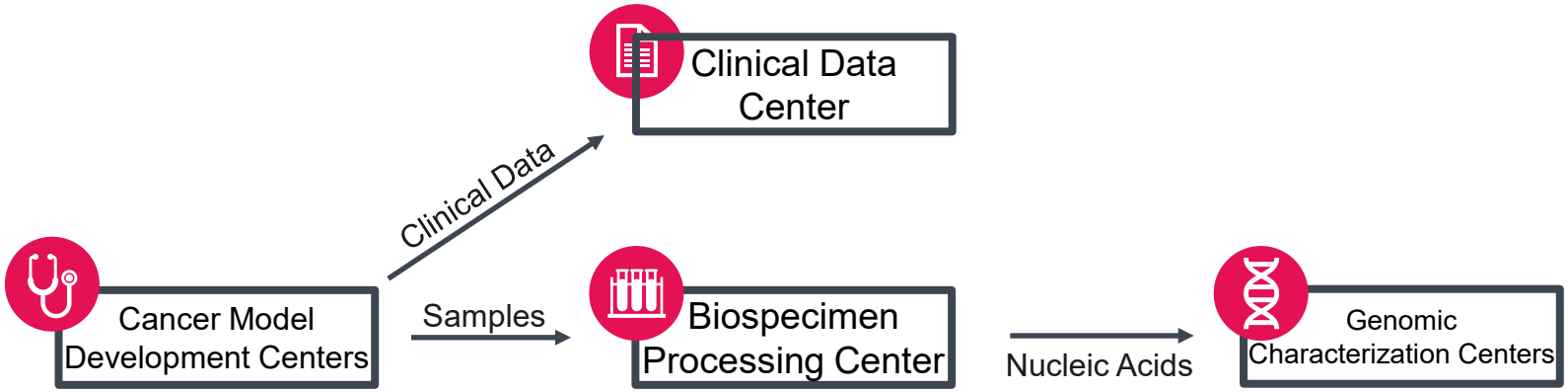


- Clinical data includes demographic information, therapeutic history, histological subtype, etc.

The Biospecimen Processing Center (BPC) processes patient tissue

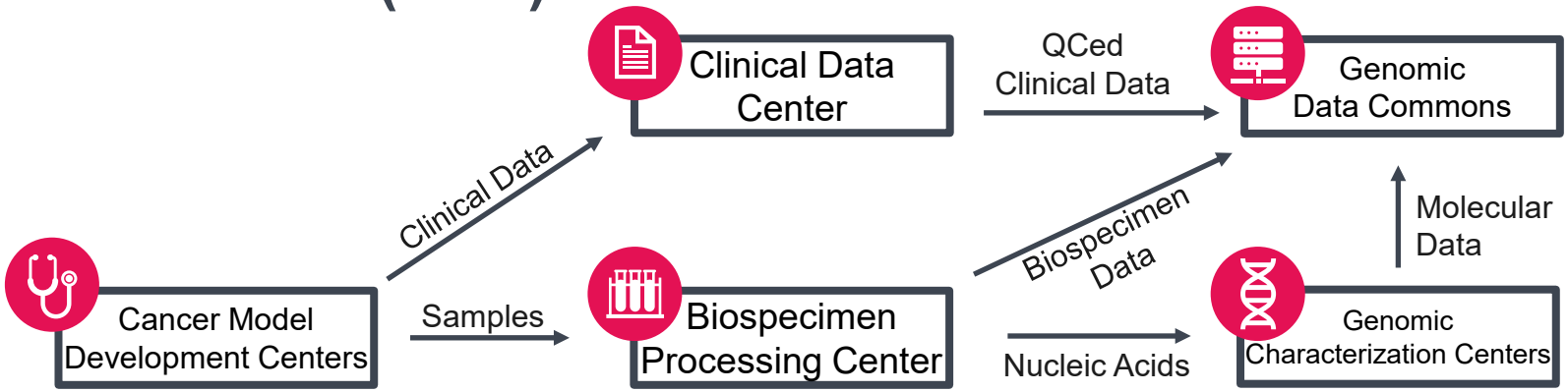


Sequencing and other molecular characterization is performed at Genomic Characterization Centers (GCCs)



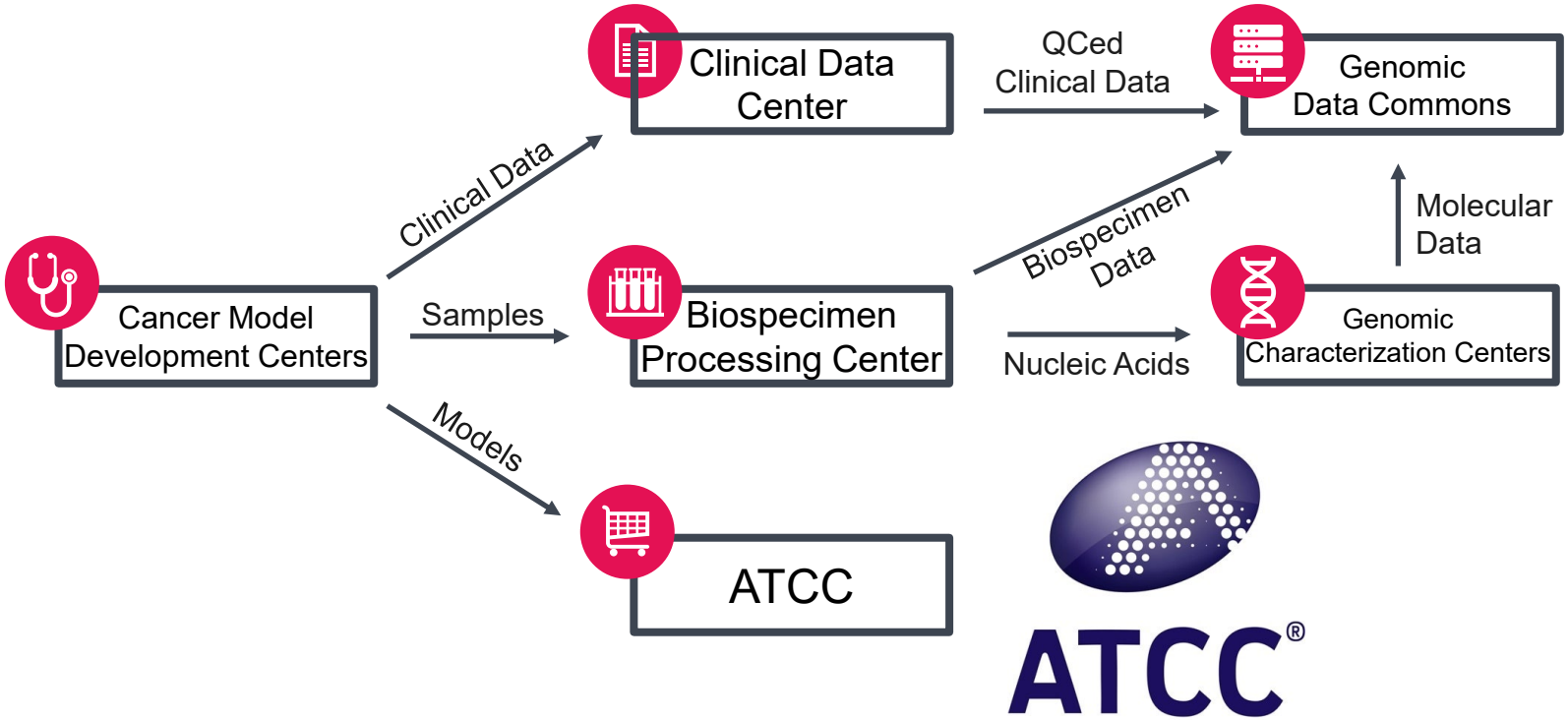
- 150x WXS and 15x WGS performed on models, tumor & normal tissue
- 120 million read RNA-seq performed on all models & tumors, and DNA methylation arrays on a subset

Harmonized & QCed data are sent to the Genomic Data Commons (GDC)

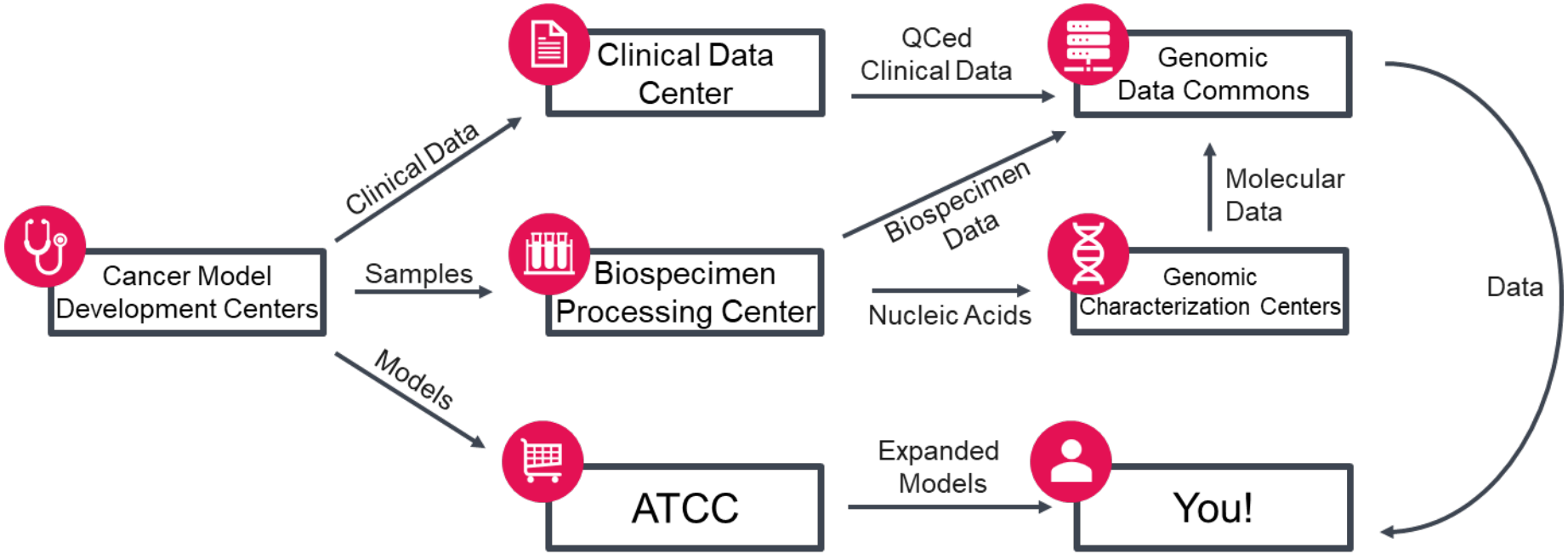


NIH NATIONAL CANCER INSTITUTE
Genomic Data Commons

Models are sent to the ATCC for expansion & distribution



Data (from GDC) and models (from ATCC) are available to the research community



- Proteomics data coming soon for some models

Outline (3)

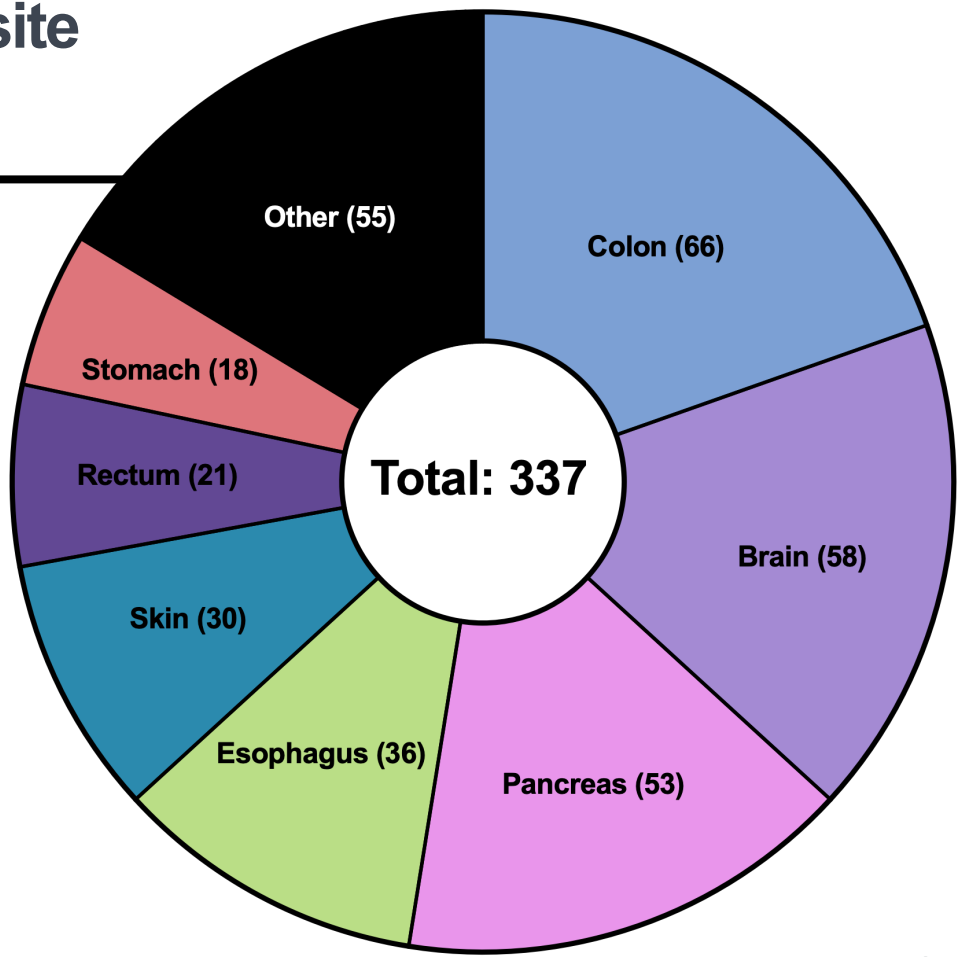
- How are models generated and quality controlled?
- **What models are available?**
- HCMI webpages & resources

HCMI models by the numbers

- ***337 models*** are currently available from ATCC, with many more in the production queue
- Data from ***664 models*** are available at the GDC
- Available models from ***32 primary sites***

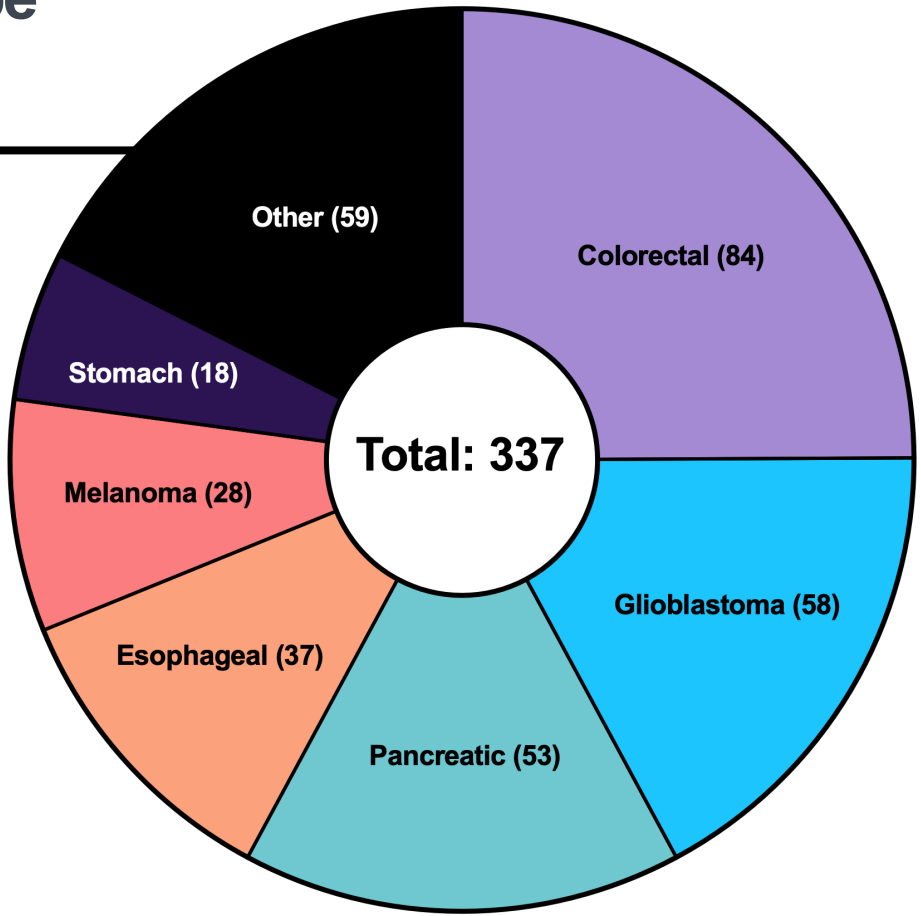
Available models by primary site

- Lung/Bronchus
- Ampulla of Vater
- Connective tissue
- Bone
- Endometrium
- Small intestine
- Extrahepatic bile duct
- Kidney
- Ovary
- Rectosigmoid junction
- Uterus
- Abdomen
- Gallbladder
- Intrahepatic bile duct
- Mouth
- Nasal cavity
- Oral cavity
- Thyroid gland
- Tongue

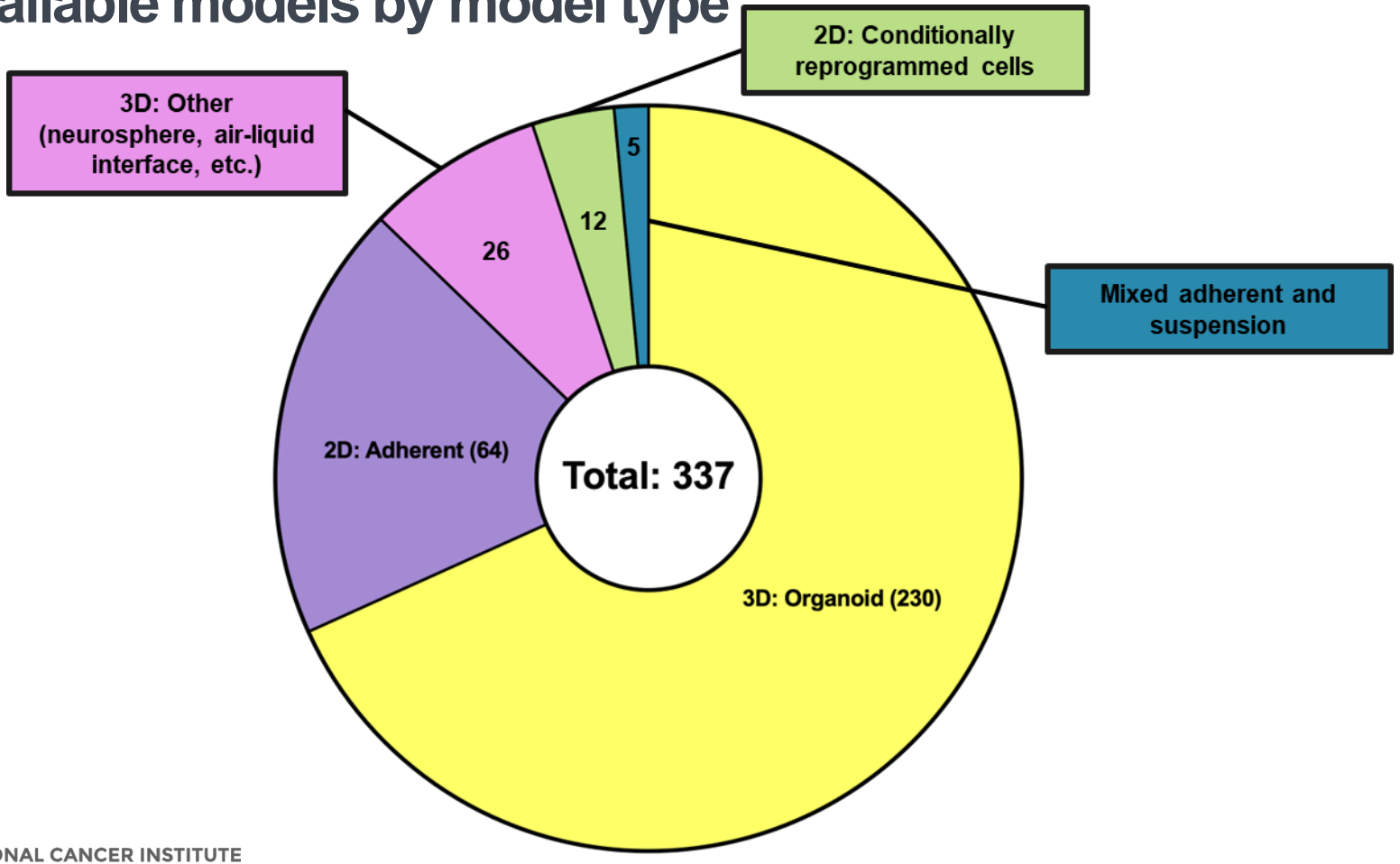


Available models by cancer type

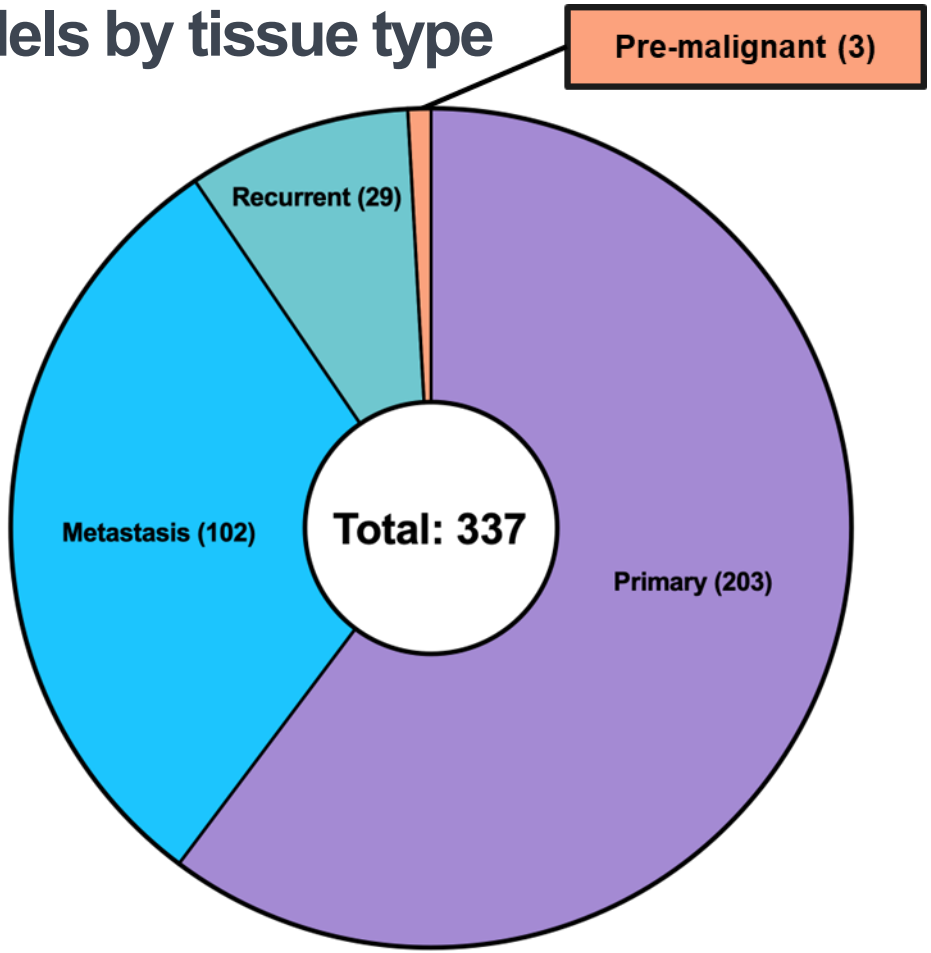
- Breast
- Endometrial
- Lung
- Ampulla of Vater
- Head & Neck
- Rhabdomyosarcoma
- Ewing's sarcoma
- Ovarian
- Wilms tumor
- Intrahepatic bile duct
- Osteosarcoma
- Others!



Available models by model type



Available models by tissue type

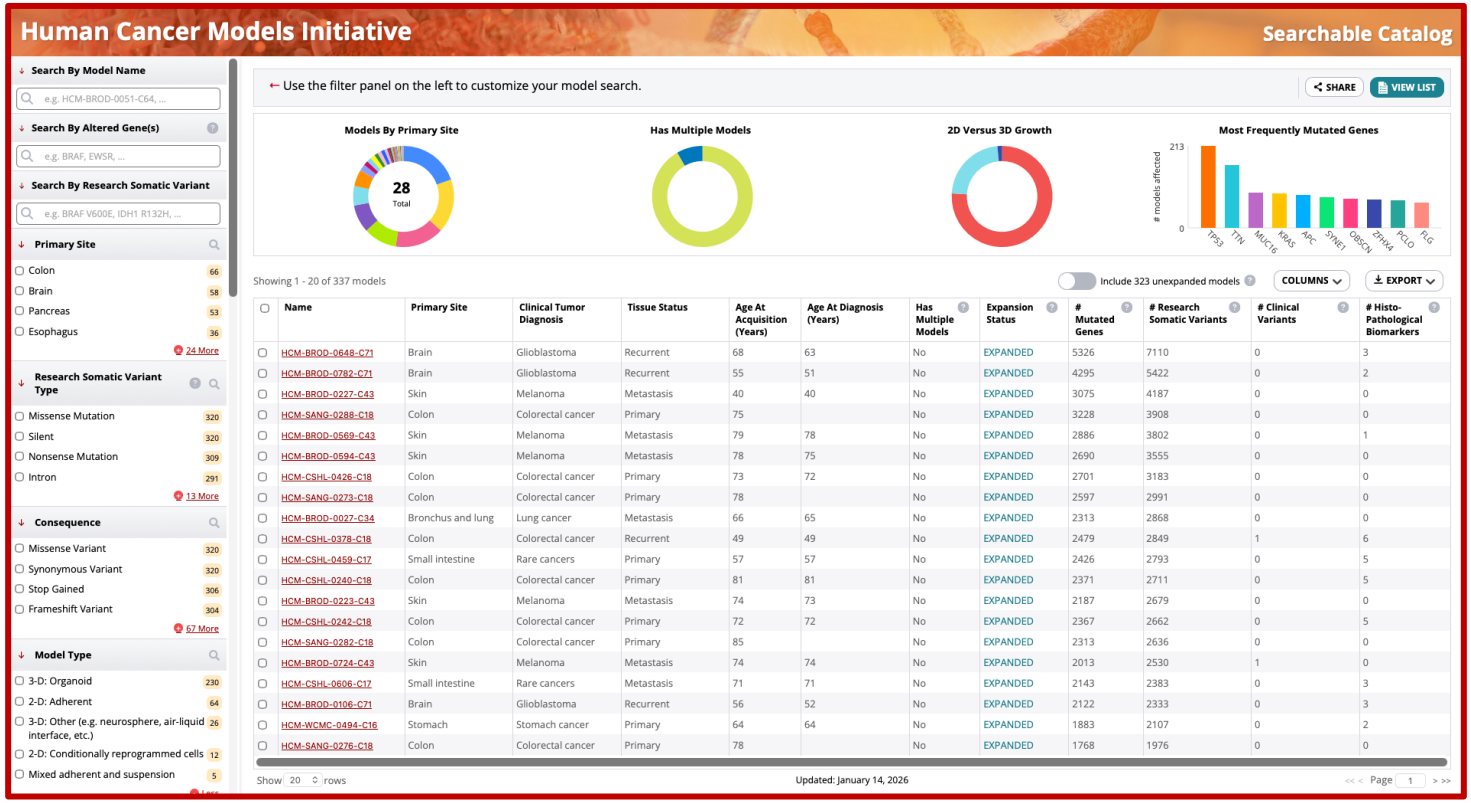


Outline (4)

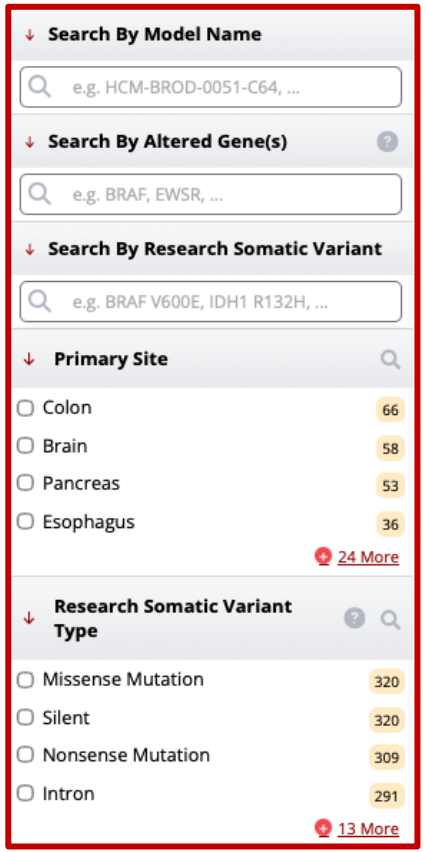
- How are models generated and quality controlled?
- What models are available?
- **HCMI webpages & resources**

HCMI Searchable Catalog

https://hcmi-searchable-catalog.nci.nih.gov



Clinical and molecular data are integrated into search



- You can filter by:
  - Primary site
  - Cancer type
  - Molecular data availability
  - Altered genes
  - Therapy history
  - More!

Model pages contain more details

Model: **HCM-CSHL-0806-C54** EXPANDED

‹ BACK TO SEARCH | ADD MODEL TO MY LIST | VIEW LIST

‹ Previous | Model 19 of 230 | Next ›

MODEL DETAILS

Model Type	**3-D: Organoid**
Split Ratio	**N/A**
Time to Split	**N/A**
Doubling Time	**N/A**
Tissue Status	**Primary**

MULTIPLE MODELS FROM THIS PATIENT (0)

There are no other models from this patient.

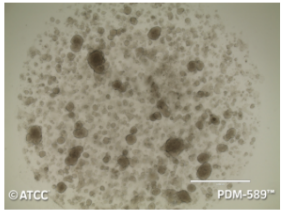
AVAILABLE MOLECULAR CHARACTERIZATIONS (10)

	Model	Tumor	Normal
WGS	✓	✓	✓
WXS	✓	✓	✓
RNA-seq	✓	✓	✗
DNA Methylation	✓	✓	✗

PATIENT DETAILS

Gender	**Female**
Race	**Black or African American**
Age At Diagnosis (Years)	**74**
Age At Acquisition (Years)	**74**
Disease Status	**No evidence of disease**
Vital Status	**Alive**
Neoadjuvant Therapy	**No**
Therapy	**• Surgery • Cytotoxic chemotherapy • Radiation therapy**
Chemotherapeutic Drug List Available	**Yes**
Clinical Tumor Diagnosis	**Endometrial cancer**
Histological Subtype	**Mixed cell carcinoma**
Primary Site	**Endometrium**
Acquisition Site	**Endometrium**
Tissue Status	**Primary**
TNM Stage	**T1bN1aMX**
Clinical Stage Grouping	**N/A**
Histological Grade	**High grade**

MODEL IMAGES (2)



Scale-bar length: 1000 µm | Magnification: 4 x

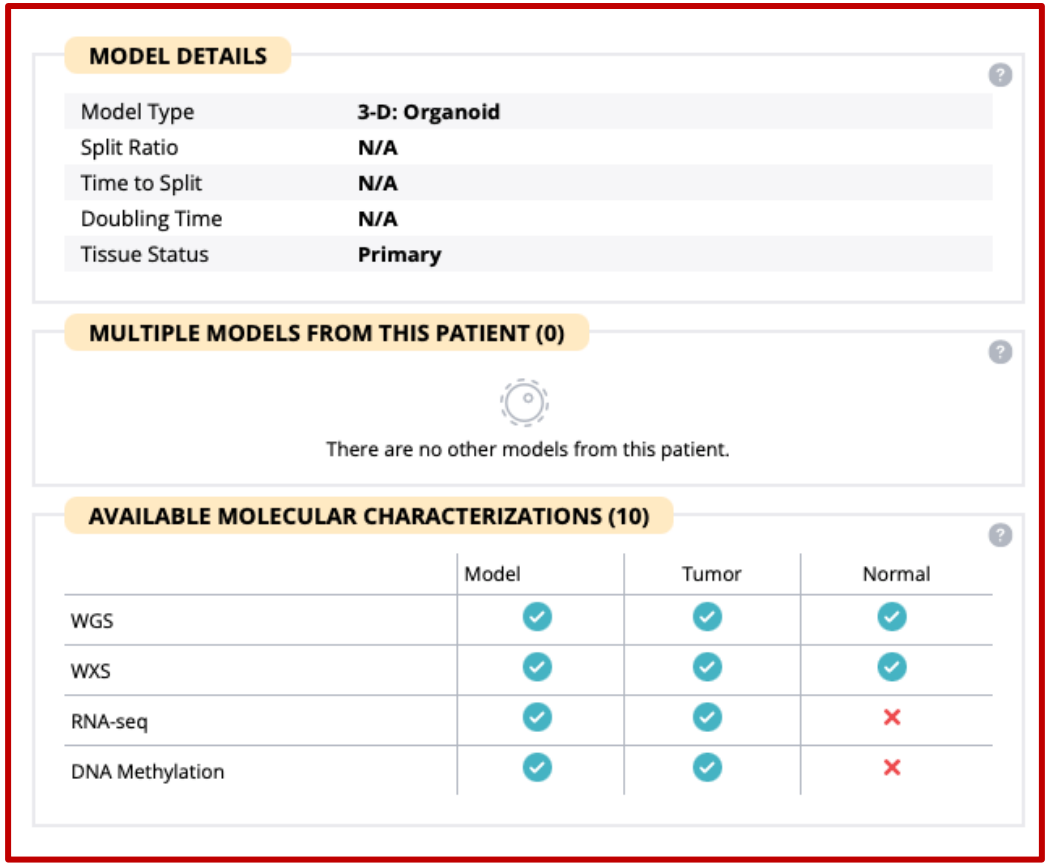
REPOSITORY STATUS

Date Updated	**May 03, 2024**
Date Of Availability	**August 31, 2023**
Licensing Required For Commercial Use	**Yes**
Date Created	**August 24, 2023**

EXTERNAL RESOURCES

SEQUENCING FILES | CASE METADATA | MASKED SOMATIC MAF | VISIT PDM-589 TO PURCHASE

Model info & available molecular data



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RNA-seq	✓	✓	✗
DNA Methylation	✓	✓	✗

Patient demographic & clinical information

PATIENT DETAILS

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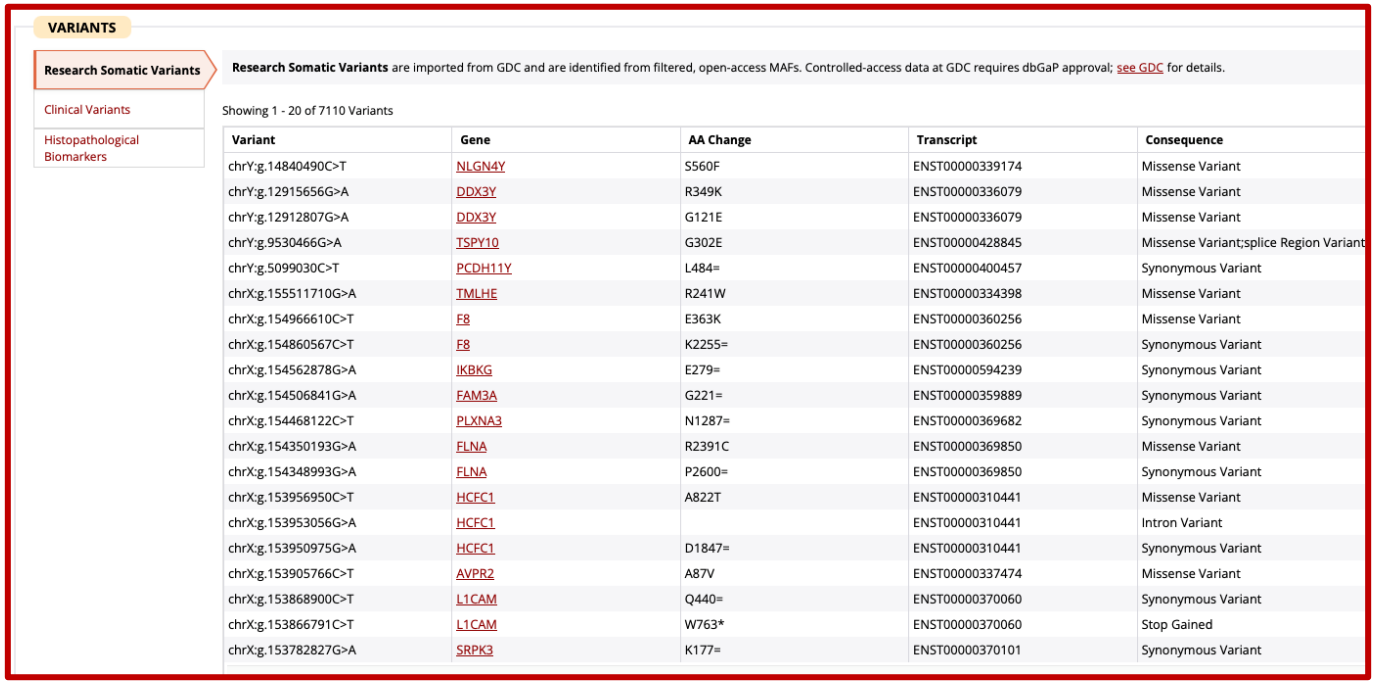
Therapy	**• Surgery** **• Cytotoxic chemotherapy** **• Radiation therapy**
Chemotherapeutic Drug List Available	**Yes**
Clinical Tumor Diagnosis	**Endometrial cancer**
Histological Subtype	**Mixed cell carcinoma**
Primary Site	**Endometrium**
Acquisition Site	**Endometrium**
Tissue Status	**Primary**
TNM Stage	**T1bN1aMX**
Clinical Stage Grouping	**N/A**
Histological Grade	**High grade**

Somatic/clinical variants and histopathological markers are imported from GDC



VARIANTS

Research Somatic Variants

Clinical Variants

Histopathological Biomarkers

Research Somatic Variants are imported from GDC and are identified from filtered, open-access MAFs. Controlled-access data at GDC requires dbGaP approval; see GDC for details.

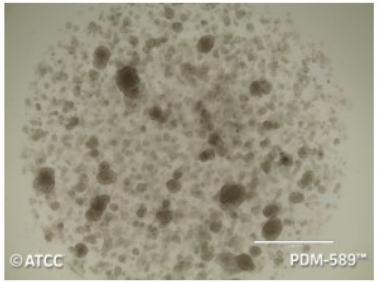
Showing 1 - 20 of 7110 Variants

Variant	Gene	AA Change	Transcript	Consequence
chrY:g.14840490C>T	NLGN4Y	S560F	ENST00000339174	Missense Variant
chrY:g.12915656G>A	DDX3Y	R349K	ENST00000336079	Missense Variant
chrY:g.12912807G>A	DDX3Y	G121E	ENST00000336079	Missense Variant
chrY:g.9530466G>A	TSPY10	G302E	ENST00000428845	Missense Variant;splice Region Variant
chrY:g.5099030C>T	PCDH11Y	L484=	ENST00000400457	Synonymous Variant
chrX:g.155511710G>A	TMLHE	R241W	ENST00000334398	Missense Variant
chrX:g.154966610C>T	F8	E363K	ENST00000360256	Missense Variant
chrX:g.154860567C>T	F8	K2255=	ENST00000360256	Synonymous Variant
chrX:g.154562878G>A	IKBKG	E279=	ENST00000594239	Synonymous Variant
chrX:g.154506841G>A	FAM3A	G221=	ENST00000359889	Synonymous Variant
chrX:g.154468122C>T	PLXNA3	N1287=	ENST00000369682	Synonymous Variant
chrX:g.154350193G>A	FLNA	R2391C	ENST00000369850	Missense Variant
chrX:g.154348993G>A	FLNA	P2600=	ENST00000369850	Synonymous Variant
chrX:g.153956950C>T	HCFC1	A822T	ENST00000310441	Missense Variant
chrX:g.153953056G>A	HCFC1		ENST00000310441	Intron Variant
chrX:g.153950975G>A	HCFC1	D1847=	ENST00000310441	Synonymous Variant
chrX:g.153905766C>T	AVPR2	A87V	ENST00000337474	Missense Variant
chrX:g.153868900C>T	L1CAM	Q440=	ENST00000370060	Synonymous Variant
chrX:g.153866791C>T	L1CAM	W763*	ENST00000370060	Stop Gained
chrX:g.153782827G>A	SRPK3	K177=	ENST00000370101	Synonymous Variant

- Full genomic data available at GDC via dbGaP

Images of each model and links to external pages

MODEL IMAGES (2)



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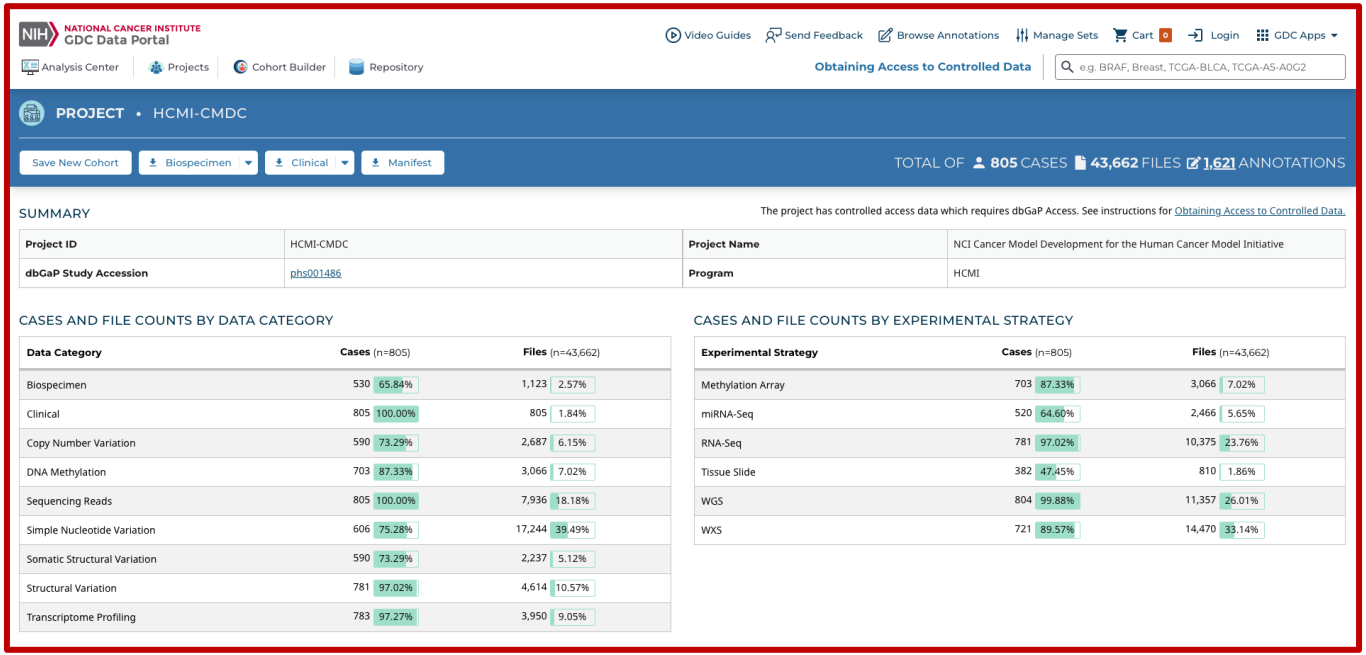
VISIT PDM-589 TO PURCHASE

GDC Data Portal: HCMI Project Page

https://portal.gdc.cancer.gov/projects/HCMI-CMDC



NIH NATIONAL CANCER INSTITUTE GDC Data Portal

Video Guides | Send Feedback | Browse Annotations | Manage Sets | Cart 0 | Login | GDC Apps

Analysis Center | Projects | Cohort Builder | Repository | Obtaining Access to Controlled Data | e.g. BRAF, Breast, TCGA-BLCA, TCGA-A5-A0G2

PROJECT • HCMI-CMDC

Save New Cohort | Biospecimen | Clinical | Manifest

TOTAL OF 805 CASES 43,662 FILES 1,621 ANNOTATIONS

SUMMARY

The project has controlled access data which requires dbGaP Access. See instructions for Obtaining Access to Controlled Data.

Project ID	HCMI-CMDC	**Project Name**	NCI Cancer Model Development for the Human Cancer Model Initiative
dbGaP Study Accession	phs001486	**Program**	HCMI

CASES AND FILE COUNTS BY DATA CATEGORY

Data Category	Cases (n=805)	Files (n=43,662)
Biospecimen	530 65.84%	1,123 2.57%
Clinical	805 100.00%	805 1.84%
Copy Number Variation	590 73.29%	2,687 6.15%
DNA Methylation	703 87.33%	3,066 7.02%
Sequencing Reads	805 100.00%	7,936 18.18%
Simple Nucleotide Variation	606 75.28%	17,244 39.49%
Somatic Structural Variation	590 73.29%	2,237 5.12%
Structural Variation	781 97.02%	4,614 10.57%
Transcriptome Profiling	783 97.27%	3,950 9.05%

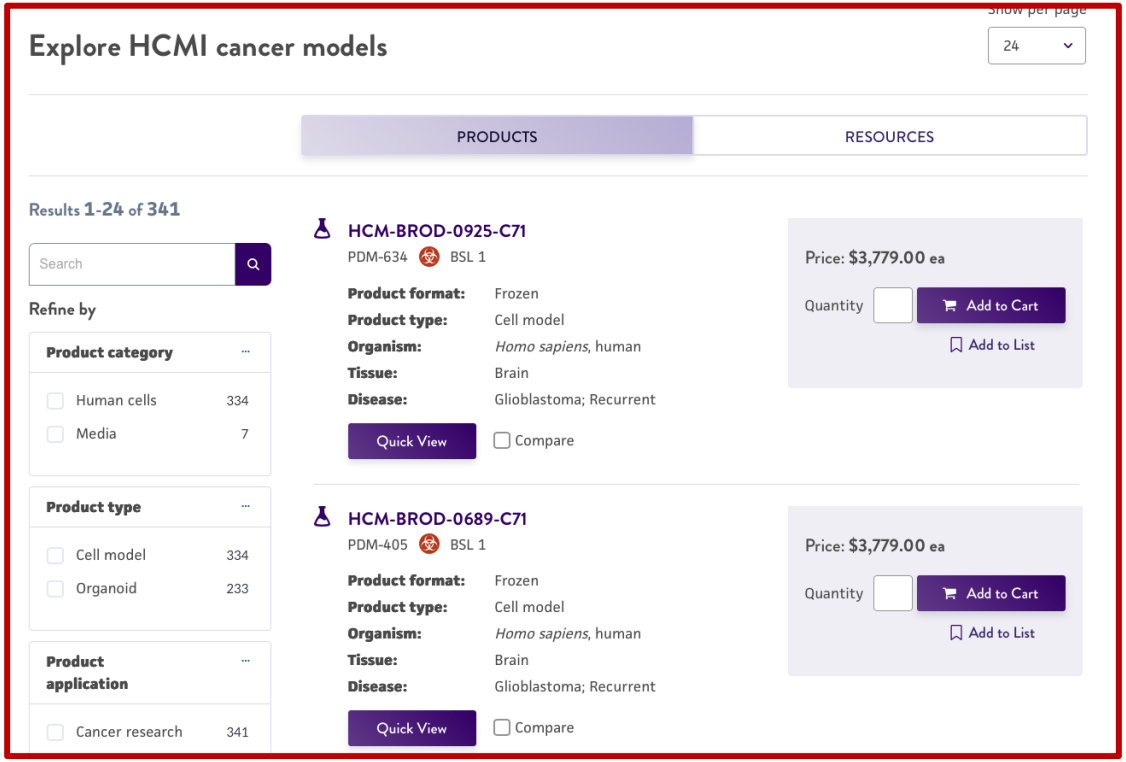
CASES AND FILE COUNTS BY EXPERIMENTAL STRATEGY

Experimental Strategy	Cases (n=805)	Files (n=43,662)
Methylation Array	703 87.33%	3,066 7.02%
miRNA-Seq	520 64.60%	2,466 5.65%
RNA-Seq	781 97.02%	10,375 23.76%
Tissue Slide	382 47.45%	810 1.86%
WGS	804 99.88%	11,357 26.01%
WXS	721 89.57%	14,470 33.14%

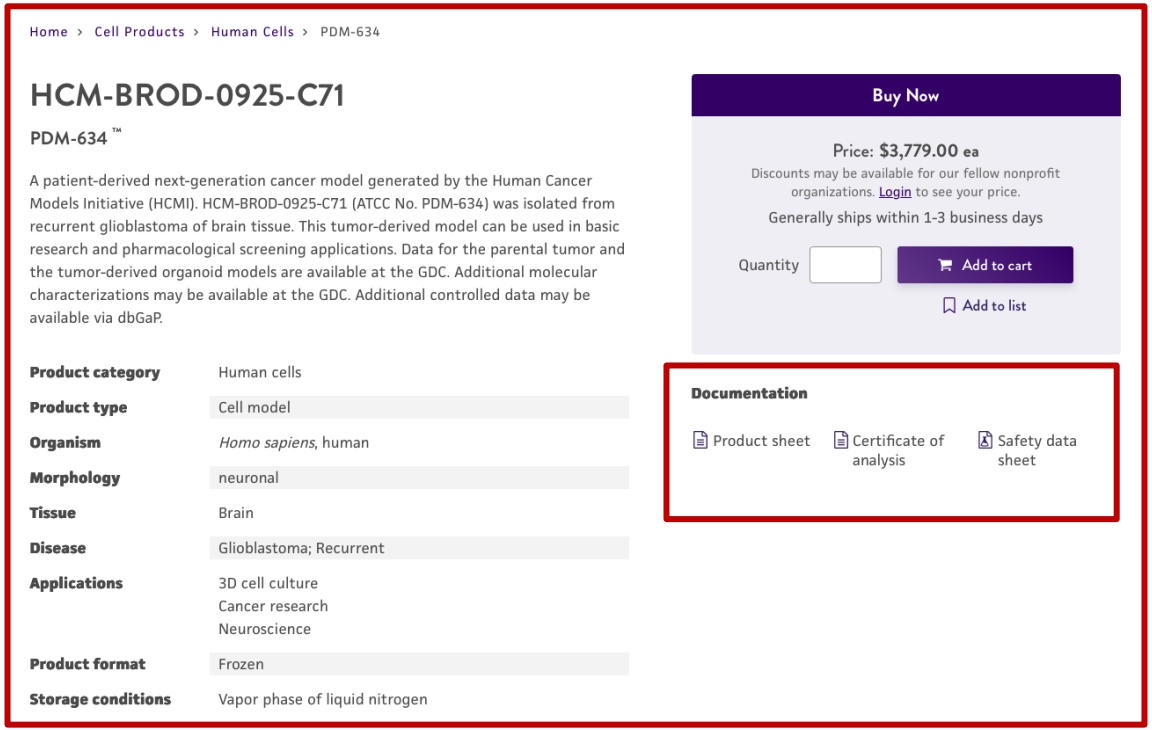
- Access controlled-access genomic data via dbGaP

ATCC Storefront

https://www.atcc.org/cell-products/collections-and-projects/human-cancer-models-initiative



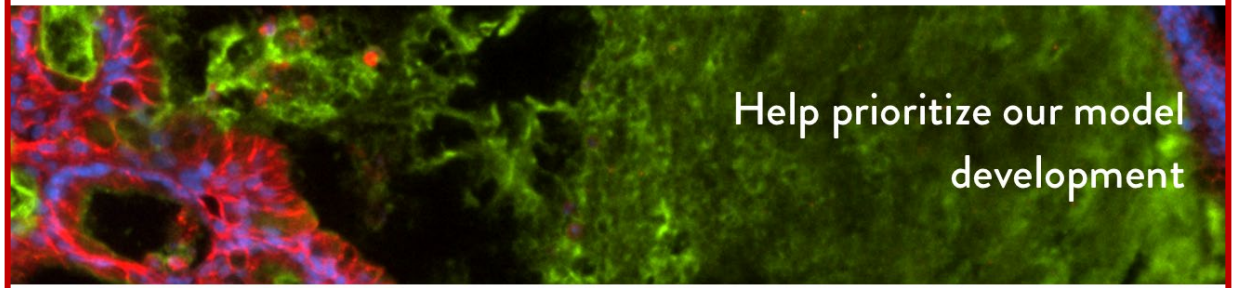
Model store page includes protocols, safety data sheet, etc.



ATCC Unmanufactured Models Page

https://www.atcc.org/hcmi-input

HCMI Unmanufactured Models



ATCC has multiple HCMI models that have not been expanded or released to the ATCC catalog; these include organoids, neurospheres, and 2-D cell models. You can give insight into which models you think should be expanded and offered for purchase. Please note that submitting your input does not guarantee that the model will ultimately be developed.

Explore the unmanufactured models below by disease state and submit your opinion using the link to the form below. To view the available clinical and molecular information, please click on the model name to view the data on the HCMI searchable catalog.

BLADDER ›
BLOOD AND LYMPHATIC SYSTEM ›
BRAIN ›
BREAST ›
CONNECTIVE/SOFT TISSUE ›
ESOPHAGUS ›
GYNECOLOGICAL TISSUE ›
HEAD AND NECK ›
KIDNEY ›
LIVER ›
LOWER DIGESTIVE TRACT ›
LUNG ›
PANCREAS ›
SKIN ›
STOMACH ›
THYROID ›

ATCC Contacts

Dr. Abhay Andar
Lead Scientist

Dr. Carolina Lucchesi
Head, Microphysiological Systems

hcmi@atcc.org

HCMI Presentations at AACR

- ***Patient-derived pediatric glioblastoma models provide key insights into IDH1-driven drug resistance***
  - Carolina Lucchesi
  - Section 30, Board 7, #6171

- ***Transcriptomic and therapeutic insights from patient-derived colorectal cancer organoids***
  - Carolina Lucchesi
  - Section 1, Board 24, #5457

- ***Next-generation models to advance pediatric solid cancer treatments***
  - Rachana Agarwal
  - Section 30, Board 2, #6166

Coming soon in *Nature…*

A Compendium of Cancer Organoid Models for Diverse Cancer Types

Dina ElHarouni, Mushriq Al-Jazrawe, Seongmin Choi, Merve Dede, Toshinori Hinoue, Sean A. Misek, Heeju Noh, Luca Zanella, Yuen-Yi Tseng, Hayley E. Francies, Dennis Plenker, Cindy W. Kyi, Julyann Perez-Mayoral, Megan J. Stine, Eva Tonsing-Carter, Rachana Agarwal, Jean Claude Zenklusen, James M. Clinton, Jennifer M. Shelton, Timothy R. Chu, William F. Hooper, Xavi Loinaz, Paula Keskula, Jordan A. Lee, Peyton C. Kuhlers, Bahar Tercan, Sylvia F. Boj, Alessandro Vasciaveo, Lorenzo Tomassoni, James M. Crawford, Shawna Walsh, Claire Sinai, Sonam Bhatia, Priya Sridevi, Hardik Patel, Maria Antonietta Cerone, The HCMI Network, Kyle Ellrott, Calvin J. Kuo, Olivier Elemento, Semir Beyaz, Vincenzo Corbo, David L. Spector, Rameen Beroukhim, Martin L. Ferguson, Andrew D. Cherniack, Peter W. Laird, Nicolas Robine, Andrew McPherson, Katherine A. Hoadley, Mathew J. Garnett, David A. Tuveson, Andrea Califano, Paul T. Spellman, Keith L. Ligon, Daniela S. Gerhard, Louis M. Staudt, Jesse S. Boehm

Thank You!

cancer.gov

cancer.gov/espanol