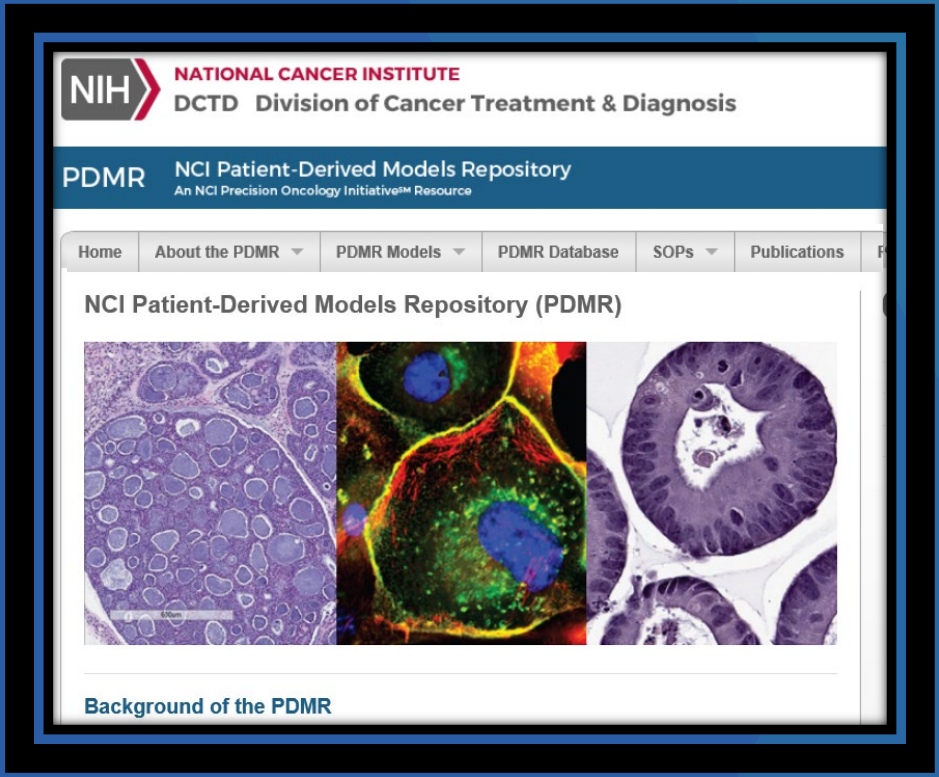

The National Cancer Institute's Patient-Derived Models Repository (PDMR)

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Frederick National Laboratory for Cancer Research

Leidos Biomedical Research, Inc. **In Support of the Division of Cancer Treatment and Diagnosis, NCI**

December 3, 2021

NCI Drug Development Workshop: How to Advance A Therapeutic Candidate from Bench to Bedside

https://pdmr.cancer.gov

Funded by NCI Contract No. HHSN261200800001E

leidos
Leidos Biomedical Research, Inc.

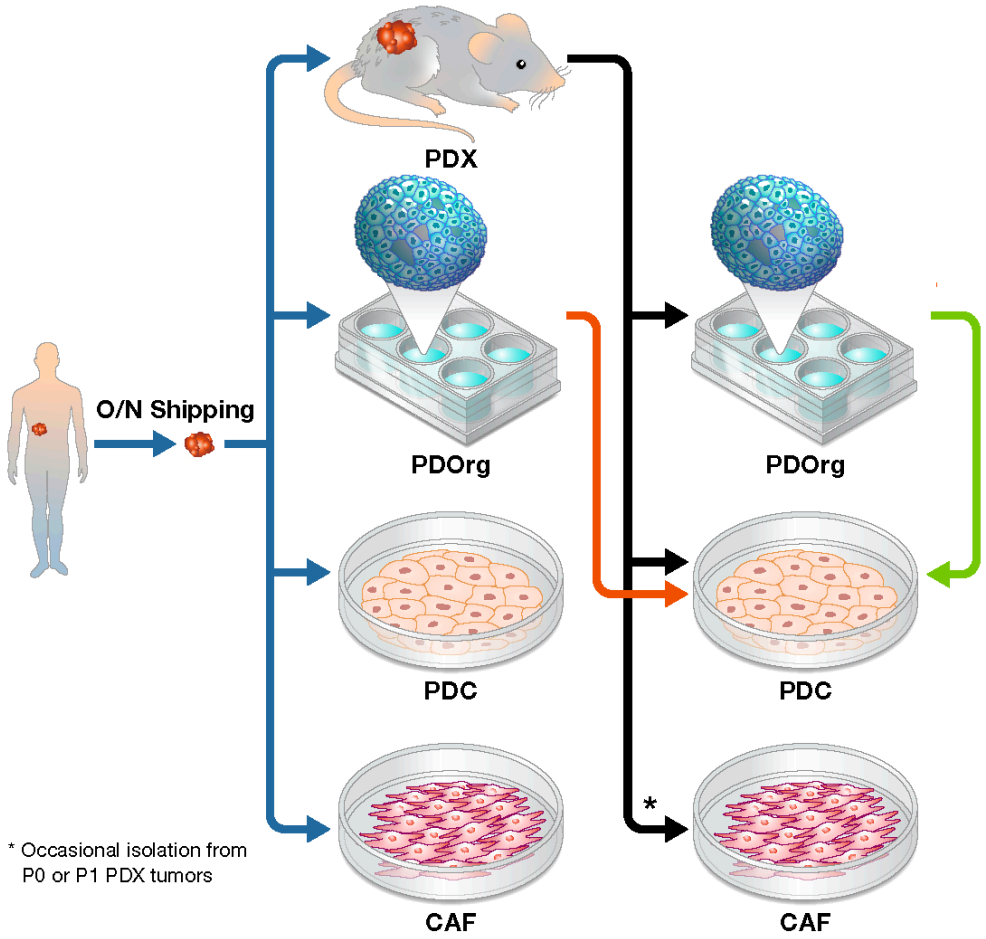
PDMR NCI Patient-Derived Models Repository
An NCI Precision Oncology Initiative℠ Resource

NIH NATIONAL CANCER INSTITUTE

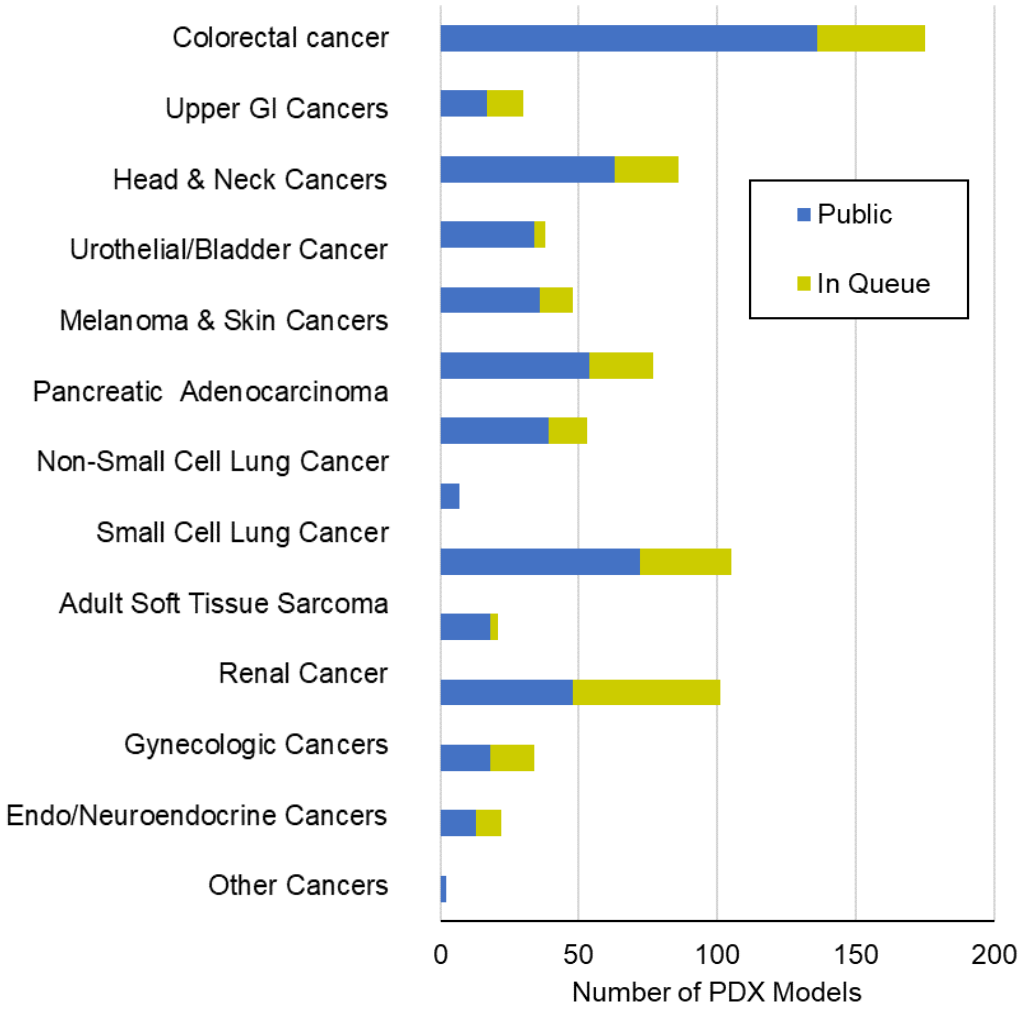
- Overview of NCI's Patient-Derived Models Repository (PDMR)
- Data Available with Models
- Summary

NCI's Patient-Derived Models Repository (PDMR)

- A national repository of Patient-Derived Models (PDMs) to serve as a resource for academic discovery efforts and public-private partnerships for drug discovery
- **Clinically-annotated** & **early-passage** models with comprehensive **molecular-characterization** and quality control metrics
- Complement existing PDM collections and focus on under-represented model types such as rare cancers and models representing racial and ethnic minorities
- Provide models to the research community at a modest cost compared to other distributors
- Provide all related metadata including: deidentified patient clinical history and outcomes, model histology, WES and RNASeq of models, and SOPs through a public website: https://pdmr.cancer.gov



Patient-Derived Xenografts (PDXs)



- **<u>576 PDX models publicly available</u>** (pdmr.cancer.gov).

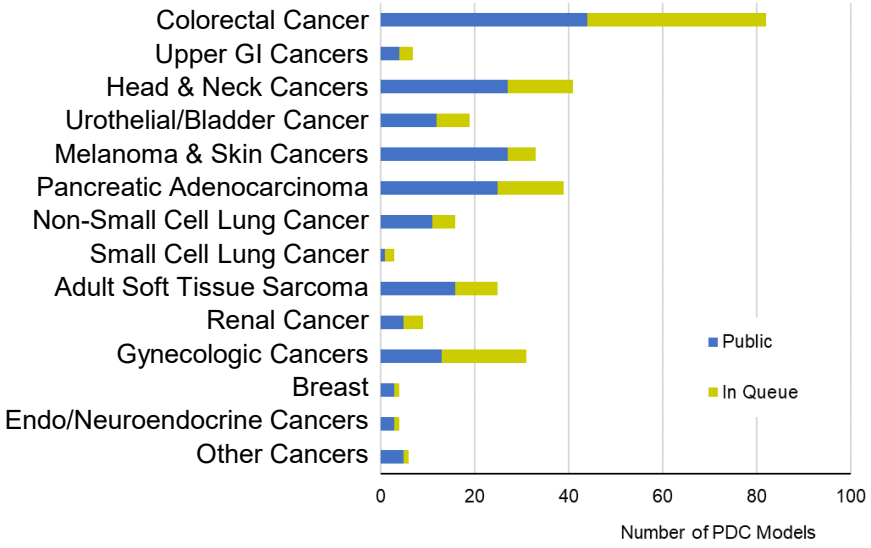
- Clinically-annotated, early-passage, molecularly-characterized patient-derived models

- **Distribution Material:**
  - ✓ LN2 cryopreserved fragments for PDX generation, FF fragments and DNA/RNA aliquots for molecular characterization
  - ✓ Median Passage = 2
    - Range for NCI-generated models: 1-8
    - Range for Contributed External models: 1-36 (P85)

- Specimens are from patients with both primary and metastatic disease from treatment naïve to heavily pre-treated.

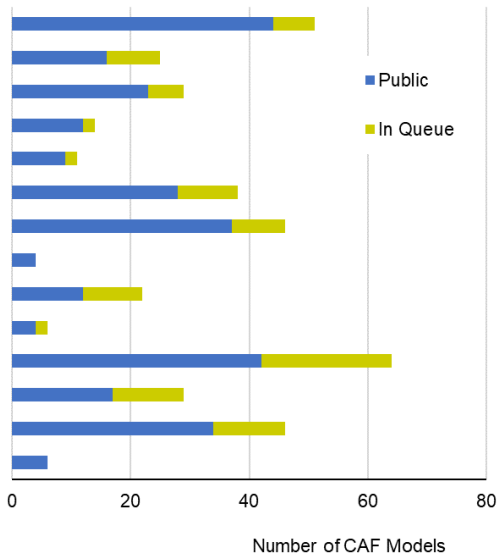
2D and 3D Patient and PDX-derived Cultures Available

196 Public PDCs



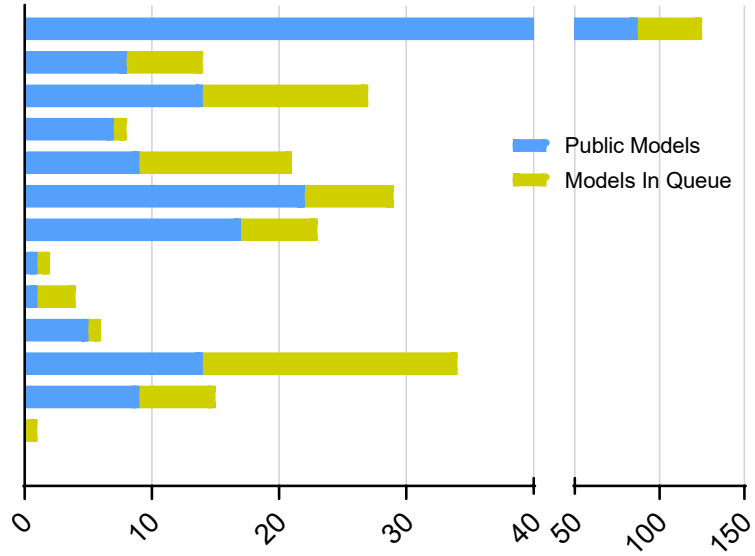
- **Adherent & Suspension Cultures**
- **Requires use of Defined Media**
- **Distribution Material**
  - ✓ Median Passage = 21
    - Range : 12-51

290 Public CAFs



- **Not Transformed - Limited Lifespan**
- **Requires use of Defined Media**
- **Distribution Material**
  - ✓ Median Passage = 14
    - Range: 9-34

204 Public PDOrgs



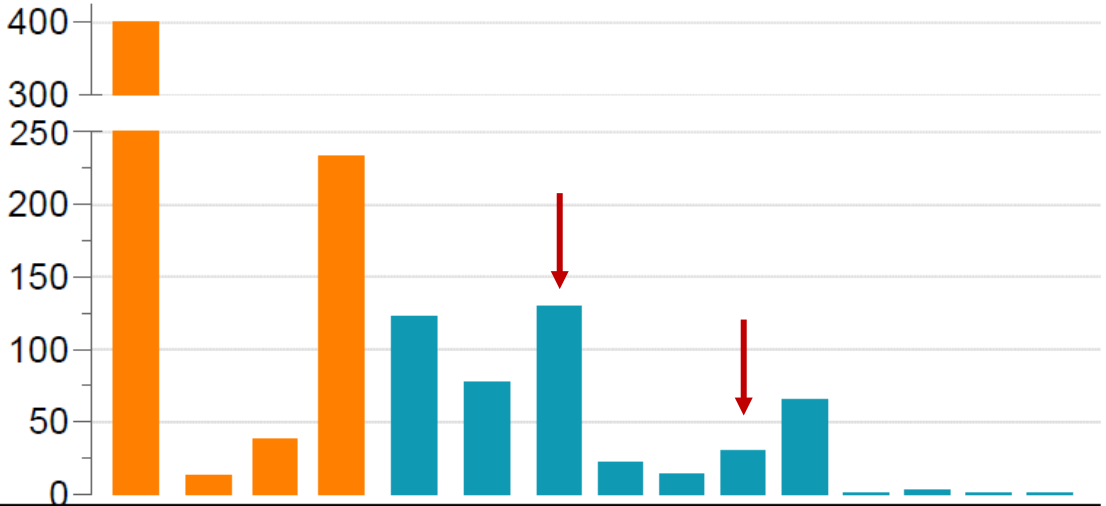
- **Requires use of defined media**
- **Distribution Material**
  - ✓ Median Passage = 12
    - Range : 4-39

- All related metadata and SOPs through the PDMR website and public database: pdmr.cancer.gov

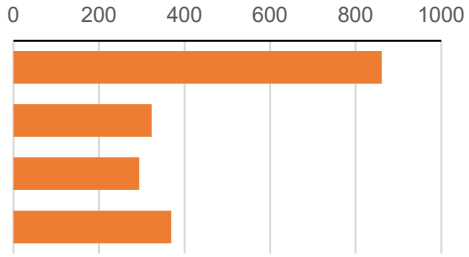
Matched PDX, PDOrg, PDC, and CAF Models

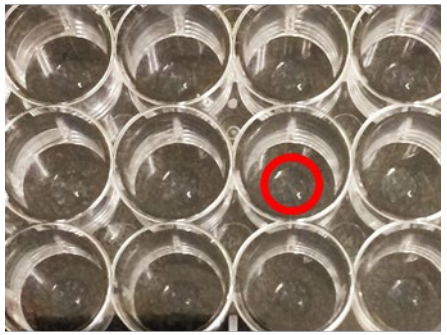
Goal: Develop a PDX, 2D *in vitro* PDC, CAF, and PDOrg culture for all models for comparative preclinical studies

Plot includes models that are either publicly available or in queue for final QC.



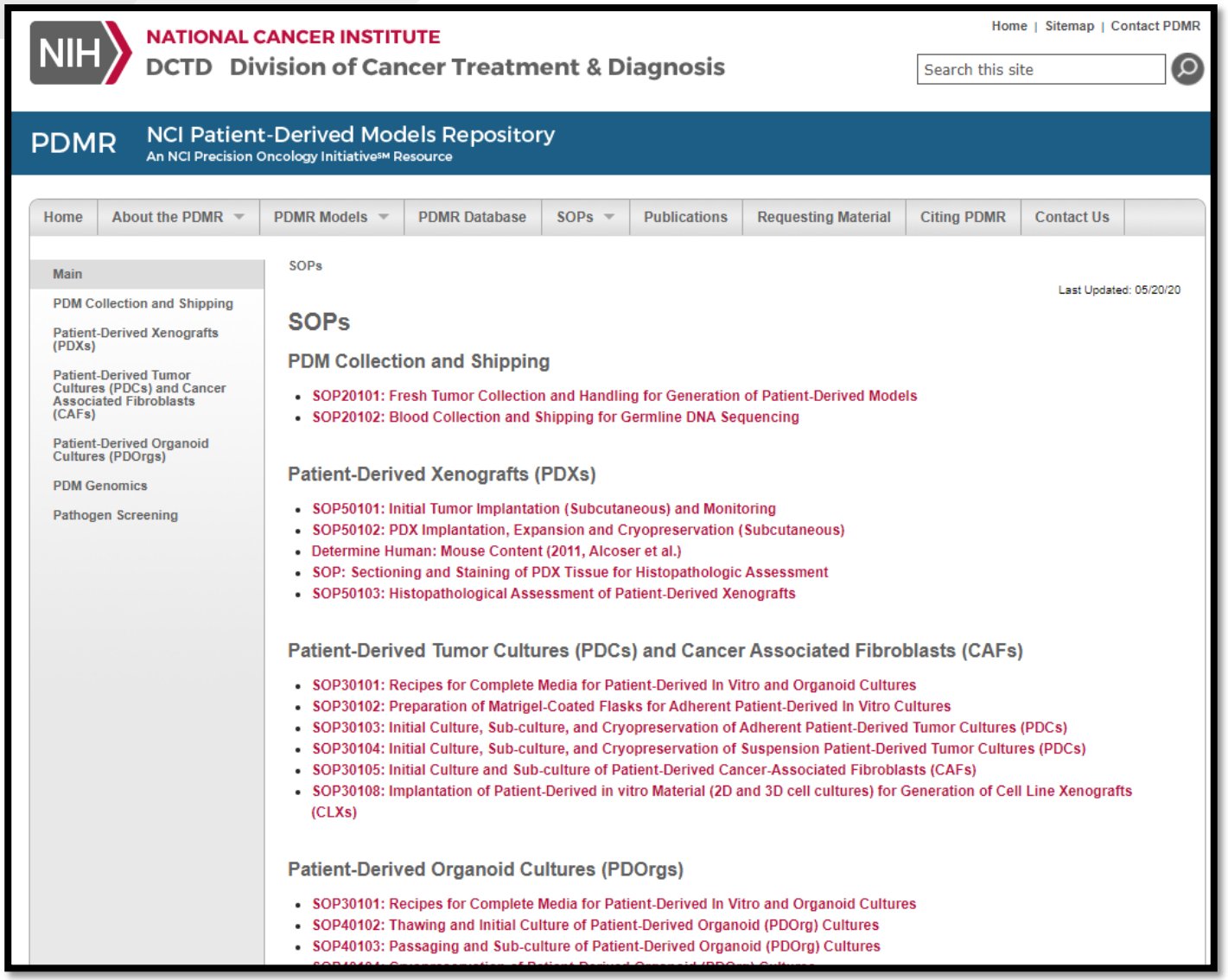
Total Individual	Total Intersect	400	13	38	233	123	77	130	22	14	30	65	1	3	1	1
861	PDX	■				■	■	■	■	■	■	■				
323	PDOrg		■			■		■	■		■		■	■	■	
294	PDC			■			■	■		■	■		■	■		■
369	CAF				■				■	■	■	■		■	■	■





Information Available in the PDMR Website and Database

SOPs



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PDMR NCI Patient-Derived Models Repository
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Home | About the PDMR | PDMR Models | PDMR Database | SOPs | Publications | Requesting Material | Citing PDMR | Contact Us

Main
PDM Collection and Shipping
Patient-Derived Xenografts (PDXs)
Patient-Derived Tumor Cultures (PDCs) and Cancer Associated Fibroblasts (CAFs)
Patient-Derived Organoid Cultures (PDOrgs)
PDM Genomics
Pathogen Screening

SOPs

Last Updated: 05/20/20

SOPs

PDM Collection and Shipping

- SOP20101: Fresh Tumor Collection and Handling for Generation of Patient-Derived Models
- SOP20102: Blood Collection and Shipping for Germline DNA Sequencing

Patient-Derived Xenografts (PDXs)

- SOP50101: Initial Tumor Implantation (Subcutaneous) and Monitoring
- SOP50102: PDX Implantation, Expansion and Cryopreservation (Subcutaneous)
- Determine Human: Mouse Content (2011, Alcoser et al.)
- SOP: Sectioning and Staining of PDX Tissue for Histopathologic Assessment
- SOP50103: Histopathological Assessment of Patient-Derived Xenografts

Patient-Derived Tumor Cultures (PDCs) and Cancer Associated Fibroblasts (CAFs)

- SOP30101: Recipes for Complete Media for Patient-Derived In Vitro and Organoid Cultures
- SOP30102: Preparation of Matrigel-Coated Flasks for Adherent Patient-Derived In Vitro Cultures
- SOP30103: Initial Culture, Sub-culture, and Cryopreservation of Adherent Patient-Derived Tumor Cultures (PDCs)
- SOP30104: Initial Culture, Sub-culture, and Cryopreservation of Suspension Patient-Derived Tumor Cultures (PDCs)
- SOP30105: Initial Culture and Sub-culture of Patient-Derived Cancer-Associated Fibroblasts (CAFs)
- SOP30108: Implantation of Patient-Derived in vitro Material (2D and 3D cell cultures) for Generation of Cell Line Xenografts (CLXs)

Patient-Derived Organoid Cultures (PDOrgs)

- SOP30101: Recipes for Complete Media for Patient-Derived In Vitro and Organoid Cultures
- SOP40102: Thawing and Initial Culture of Patient-Derived Organoid (PDOrg) Cultures
- SOP40103: Passaging and Sub-culture of Patient-Derived Organoid (PDOrg) Cultures

Deidentified Patient Data & PDX Model Data

* Patient ID	112475
Gender	<Unknown> Male Female
Disease Body Location	Gynecologic
CTEP SDC Code	10033159 - Ovarian epithelial cancer
Diagnosis Subtype	Papillary Serous Cystadenocarcinoma
Date of Diagnosis	04/2009
Age at Diagnosis	67

Limited Medical Information (provided after delinking)

Current Therapy

View	Date Regimen Started	Standardized Regimen	Best Response	Number of Cycles	Date of Progression or Off Therapy	Comments	Reason for Off Therapy
		No Current Therapy	NA	0			

Prior Therapies and Response

View	Date Regimen Started	Standardized Regimen	Best Response	Duration Months	Comments
	05/2009	Carboplatin, Paclitaxel	PR	9	
	06/2010	Bevacizumab, Carboplatin, Paclitaxel	PR	1	
	11/2010	Bevacizumab	Disease Progression	8	
	08/2012	Carboplatin, Gemcitabine	Disease Progression	5	
	08/2012	Paclitaxel	Stable Disease	20	
	07/2013	Bevacizumab, Pemetrexed	Disease Progression	3	

Disease Body Location	Gynecologic	Human Pathogen Testing Summary	Negative
CTEP SDC Code	10033159 - Ovarian epithelial cancer	Specimen Notes	PDX IHC/Path: ER+, PR+ PDX Growth Characteristics: Estradiol not required for growth
Tissue Type	Resection	Able to Viably Passage into Athymic Nude Mice?	Yes
Tissue Collected	Peritoneum	Mouse Strain Used for Engraftment	NSG (NOD.Cg-Prkdc[scid]Il2rg[tm1Wjl]/SzJ)
Provided Tissue Origin	Metastatic Site	Viable Passage Implantation Site	Subcutaneous (flank)
Collection Date	04/2016	MSI Status	MSI-Stable
Age at Sampling	73	Metastatic in NSG?	Not Observed

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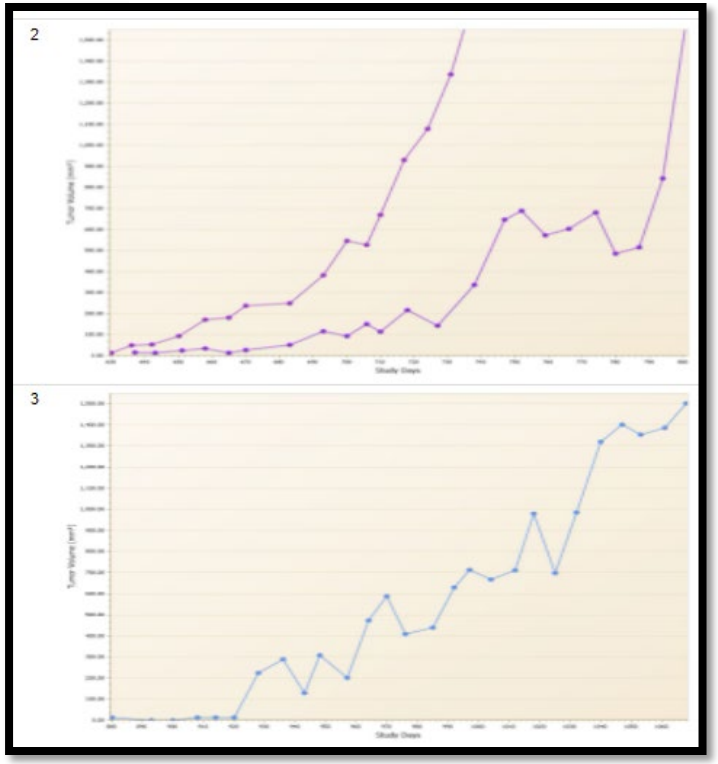
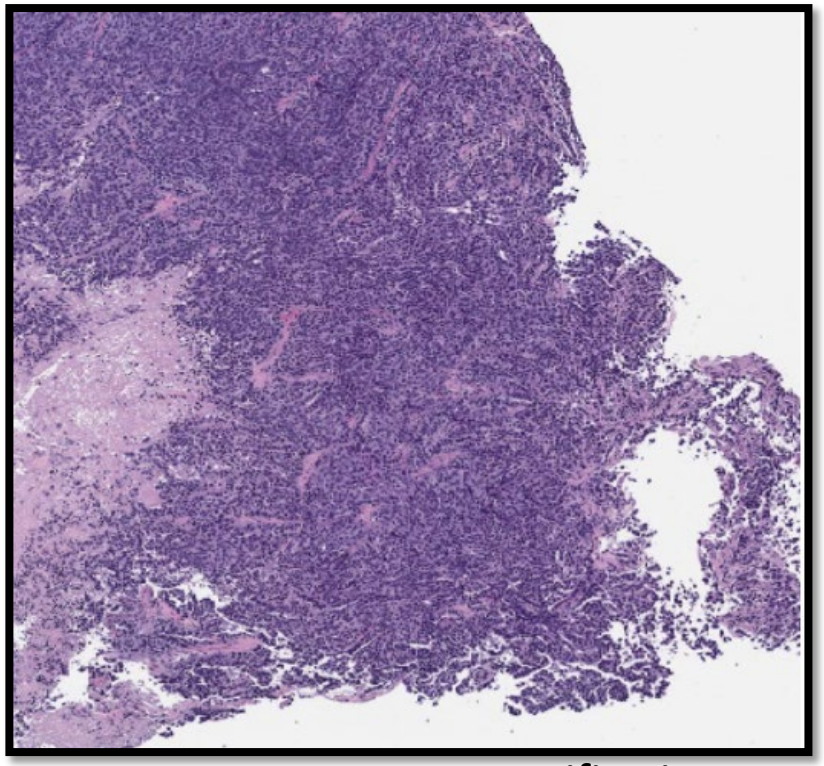
PDXs: Representative Growth Curves and H&E Images

Tumor Grade	High grade or poorly differentiated
Tumor Content	40 %
Necrosis	50 %
Stromal	10 %
Inflammatory Cell	1+ (Low)

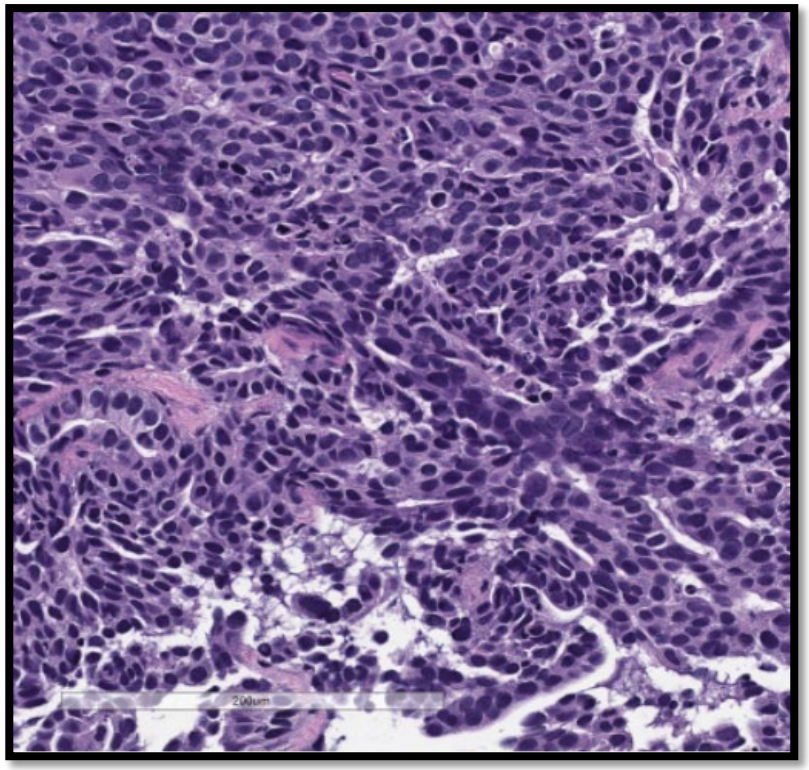
Pathology Notes

Papillary serous carcinoma of the ovary.
The section shows compact ovarian epithelial growth in solid sheets and papillary pattern at periphery. The tumor cells are flat, some of them have bubbly to clear cytoplasm, with high nuclear to cytoplasmic ratio and marked pleomorphism of the nucleus. Occasional multinucleated tumor giant cells are noted. Mitotic figures and necrosis are noted.





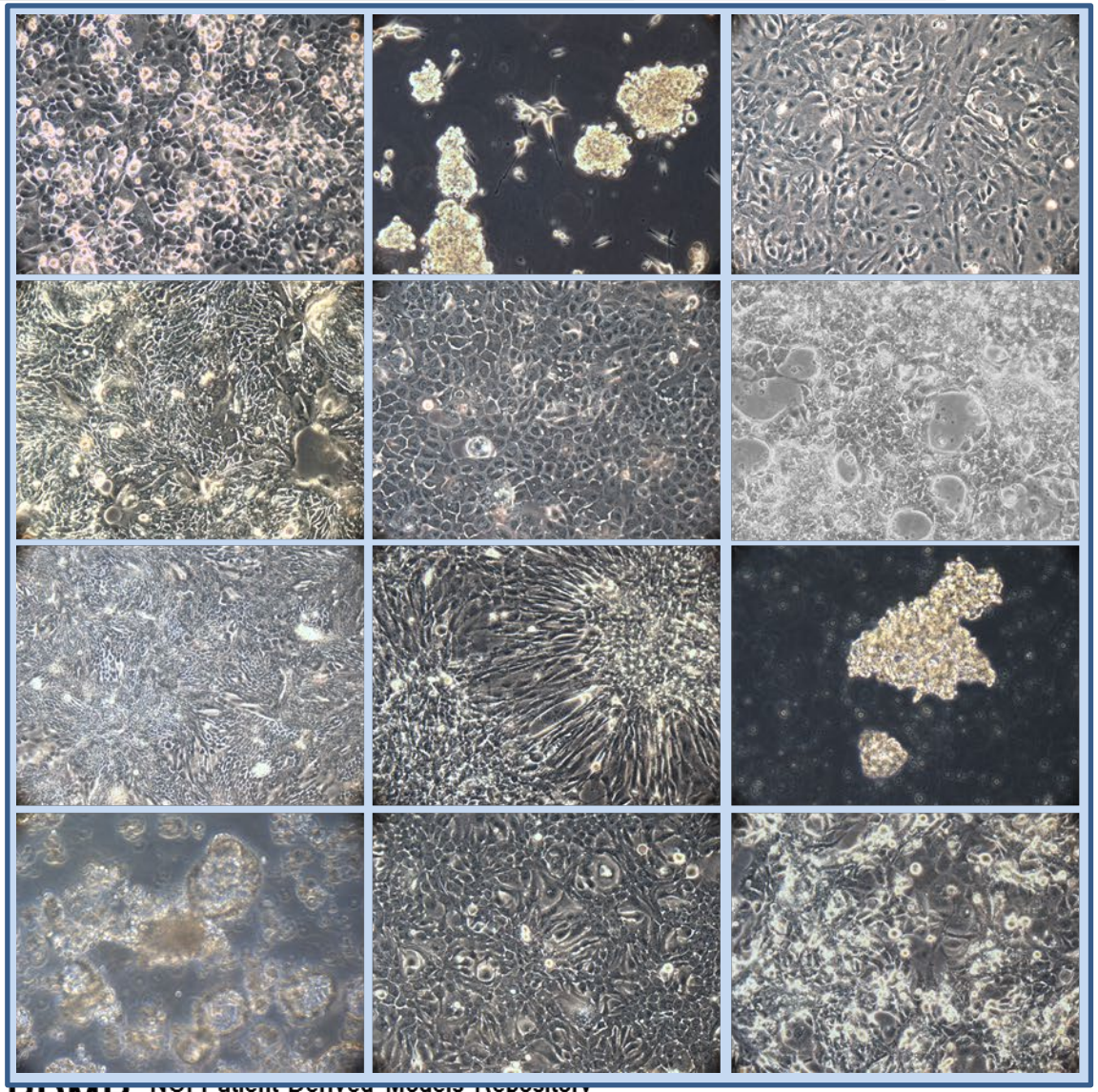
Low Magnification



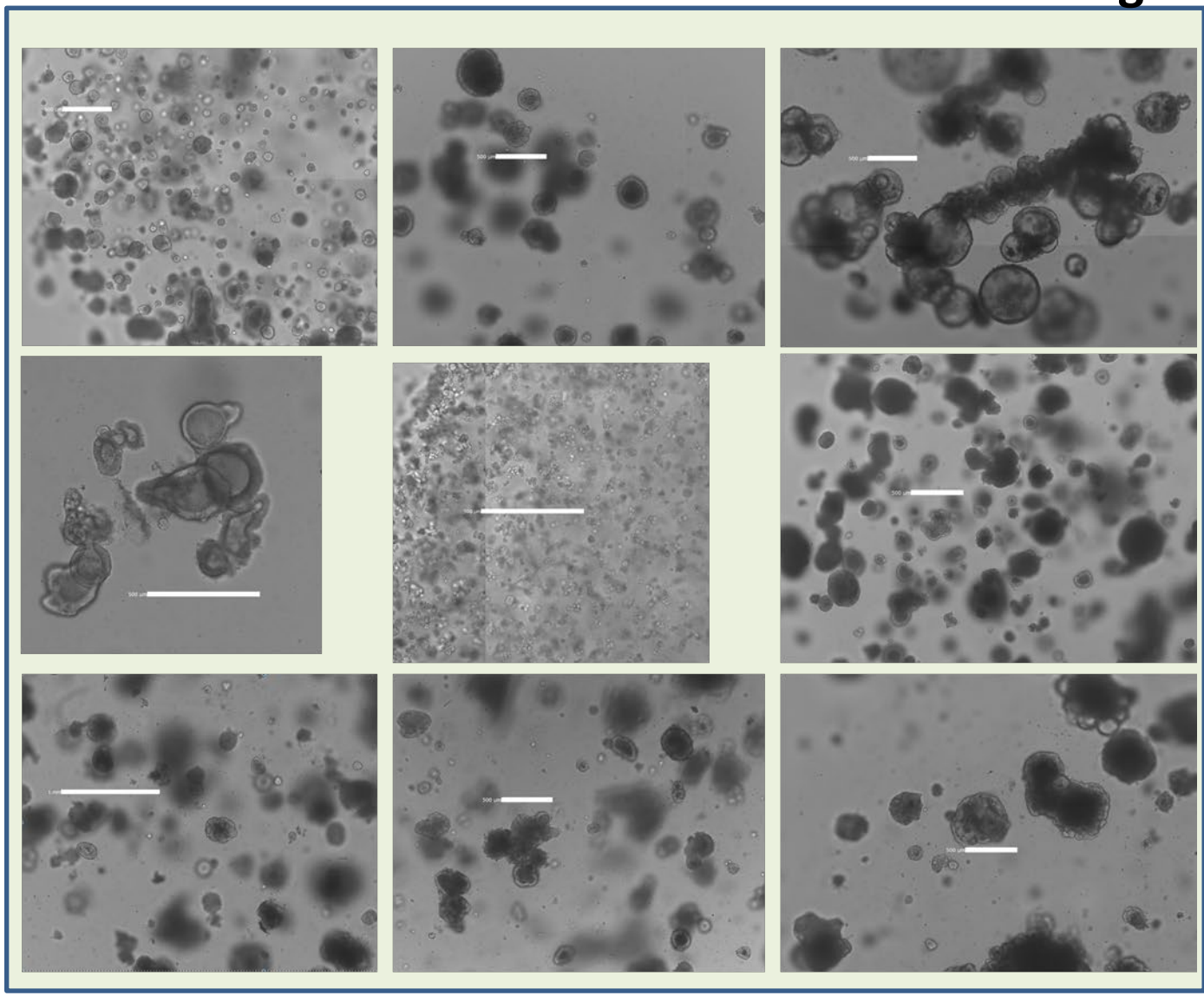
High Magnification

In vitro Cultures: Representative Culture and Cell Line Xenograft (CLX) H&E Images

PDCs

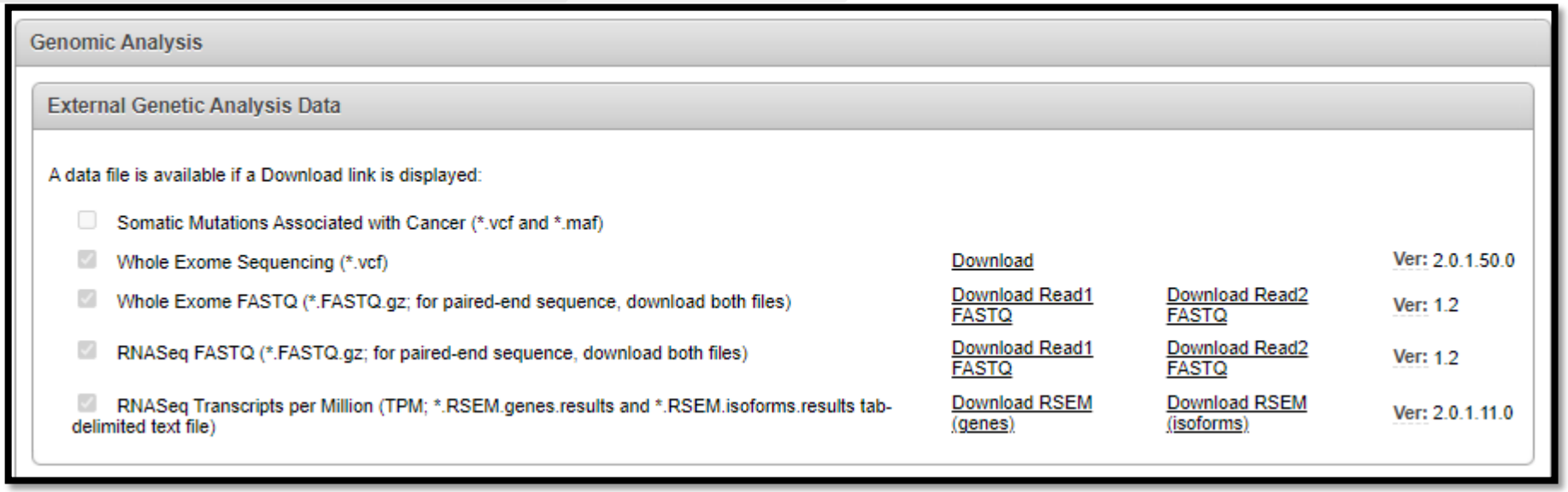


PDOrgs



500um

OncoKB mutations, WES and RNASeq files

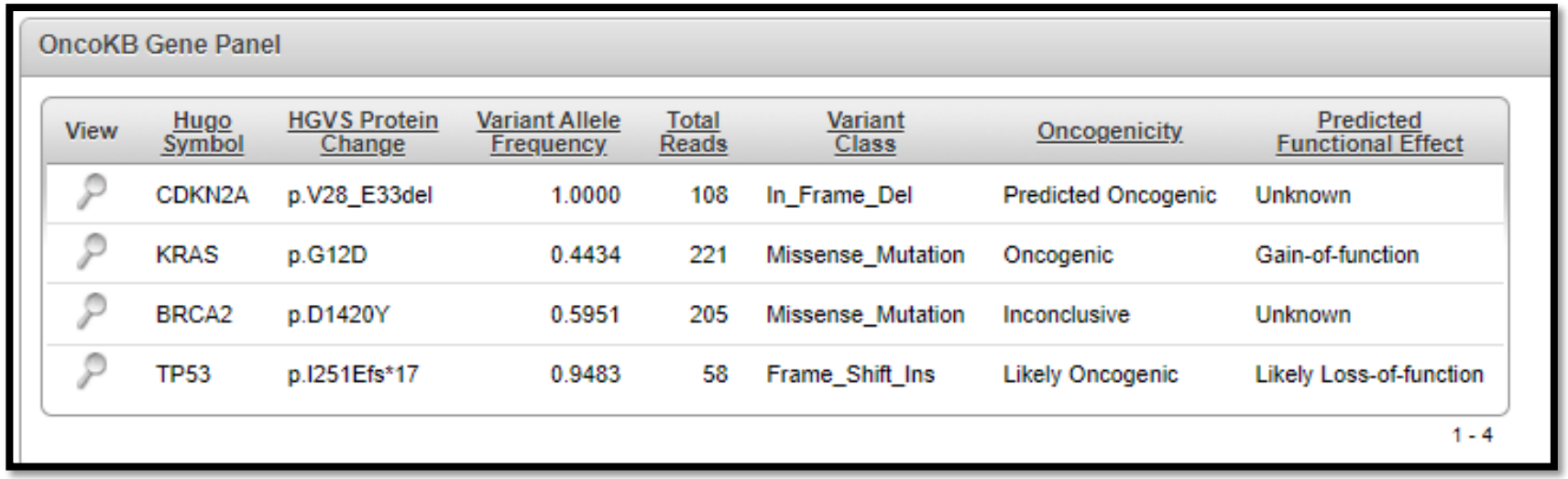


Genomic Analysis

External Genetic Analysis Data

A data file is available if a Download link is displayed:

Somatic Mutations Associated with Cancer (*.vcf and *.maf)			
Whole Exome Sequencing (*.vcf)	Download		Ver: 2.0.1.50.0
Whole Exome FASTQ (*.FASTQ.gz; for paired-end sequence, download both files)	Download Read1 FASTQ	Download Read2 FASTQ	Ver: 1.2
RNASeq FASTQ (*.FASTQ.gz; for paired-end sequence, download both files)	Download Read1 FASTQ	Download Read2 FASTQ	Ver: 1.2
RNASeq Transcripts per Million (TPM; *.RSEM.genes.results and *.RSEM.isoforms.results tab-delimited text file)	Download RSEM (genes)	Download RSEM (isoforms)	Ver: 2.0.1.11.0



OncoKB Gene Panel

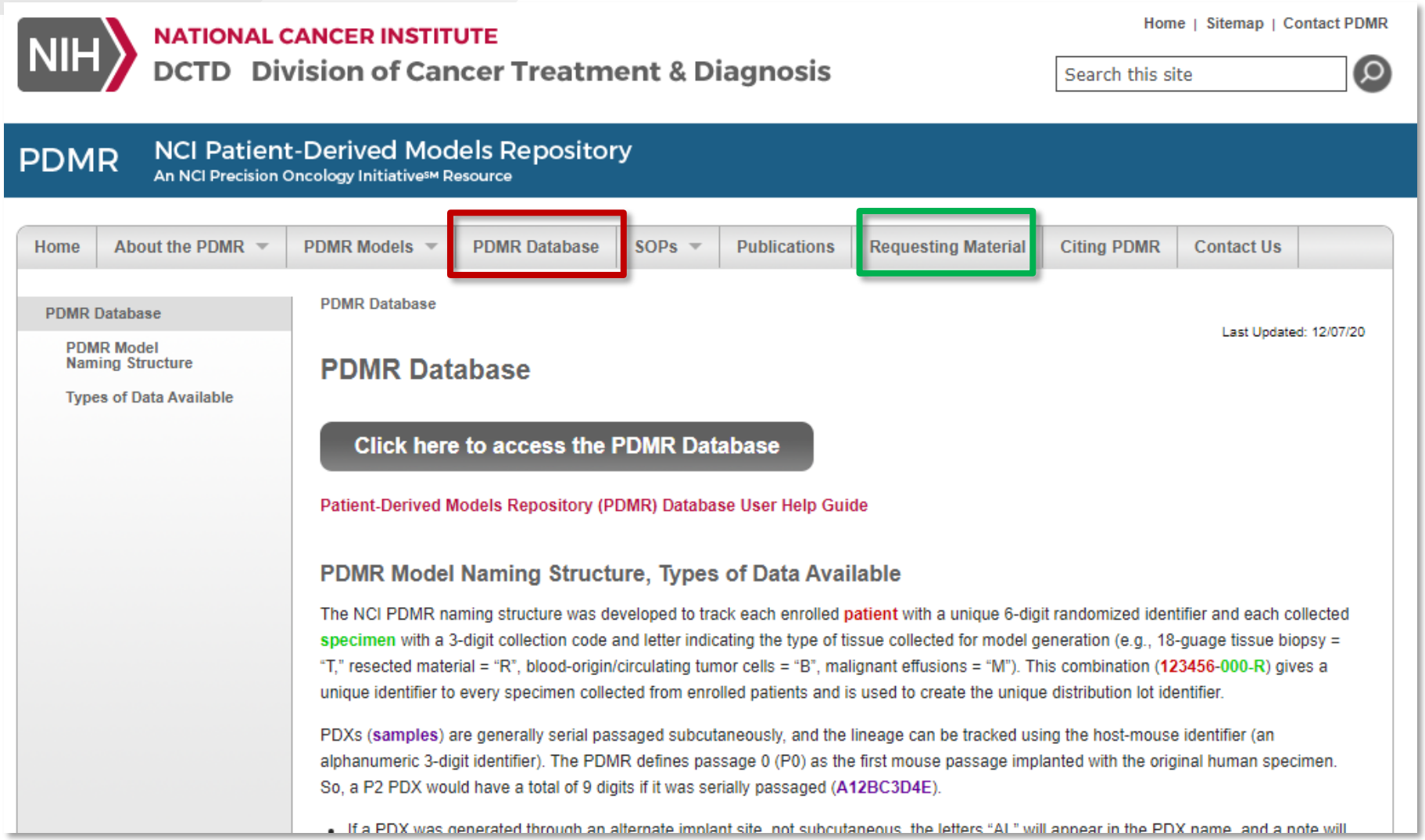
View	Hugo Symbol	HGVS Protein Change	Variant Allele Frequency	Total Reads	Variant Class	Oncogenicity	Predicted Functional Effect
	CDKN2A	p.V28_E33del	1.0000	108	In_Frame_Del	Predicted Oncogenic	Unknown
	KRAS	p.G12D	0.4434	221	Missense_Mutation	Oncogenic	Gain-of-function
	BRCA2	p.D1420Y	0.5951	205	Missense_Mutation	Inconclusive	Unknown
	TP53	p.I251Efs*17	0.9483	58	Frame_Shift_Ins	Likely Oncogenic	Likely Loss-of-function

1 - 4

Summary

- In development:
  - PDX development for AML, ALL, MDS and other leukemias
  - HLA-typing of PDX models
  - Fusions in PDMR models
- Over 800 PDX models across all solid tumor histologies have been developed to date, 576 currently publicly available
  - A large number of these are from rare and recalcitrant cancer
- Targeted effort to develop matched PDC and PDOrg models for all PDXs
- Identification of metastatic models during the model development process are being fed into a whole mouse imaging effort to characterize and upload to TCIA

Ordering Models or Reviewing Associated Data



https://pdmr.cancer.gov

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