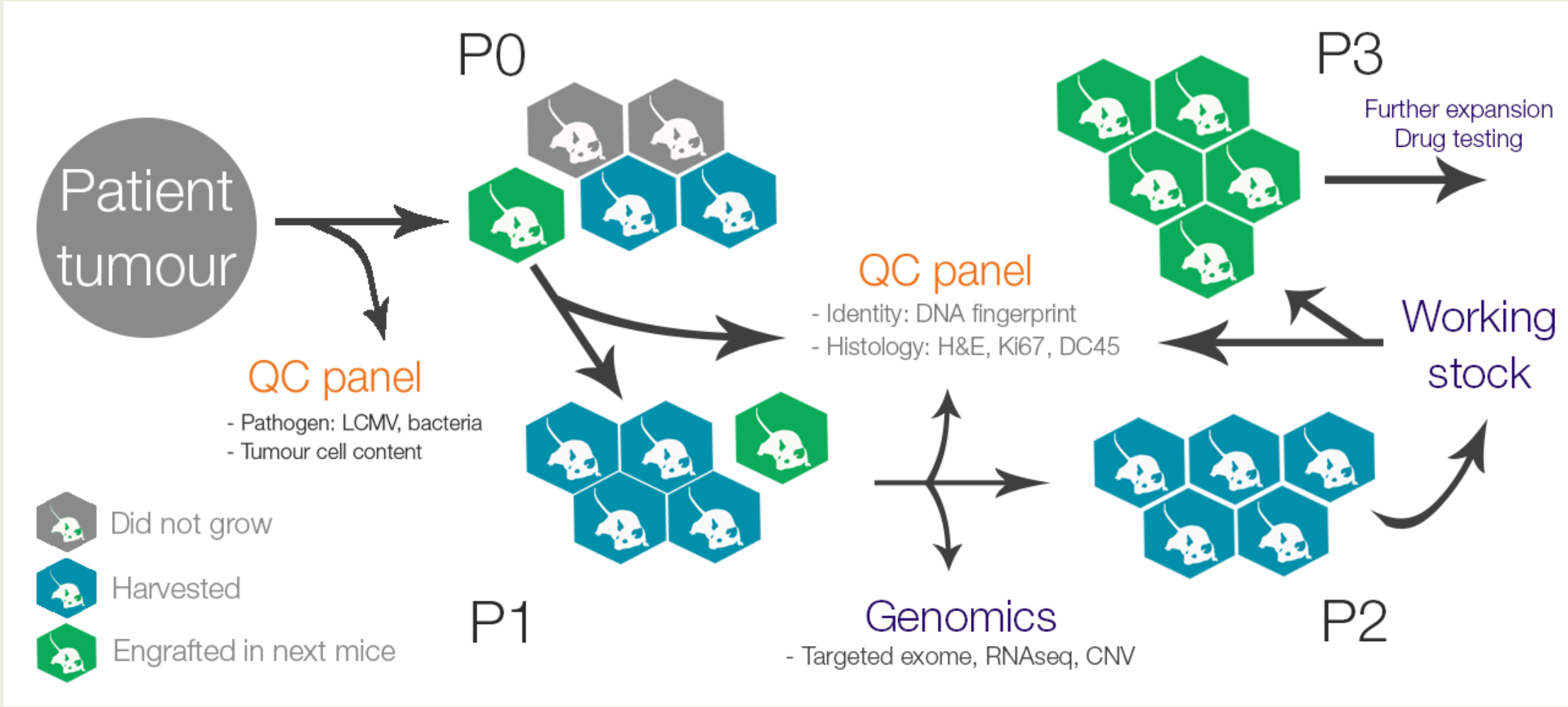
PDX FINDER

Terry Meehan

Coordinator Mouse Informatics

EMBL-EBI, Cambridge UK

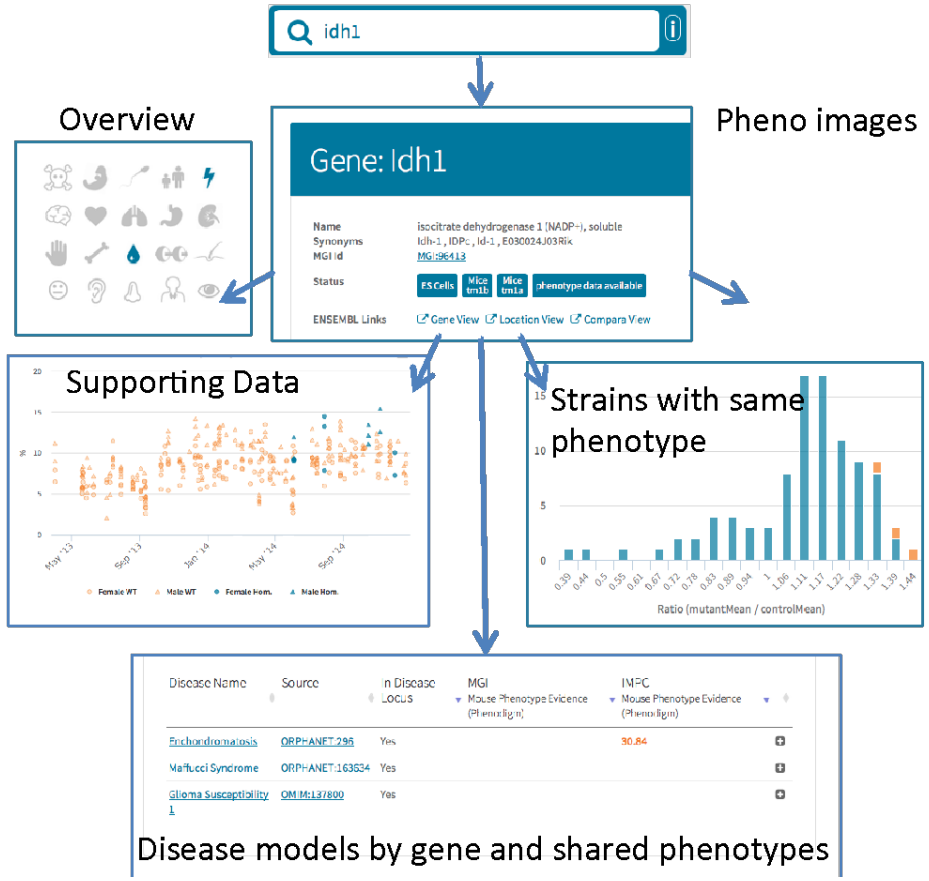
PATIENT TUMOR DERIVED XENOGRAFT MODELS



Modified from

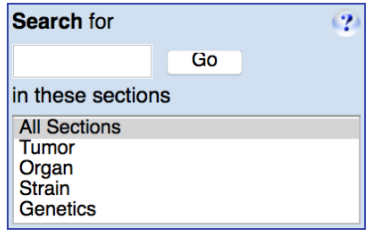
KOMP2 / IMPC & MOUSE TUMOR DATABASE

Search for gene, phenotypes, disease, anatomy

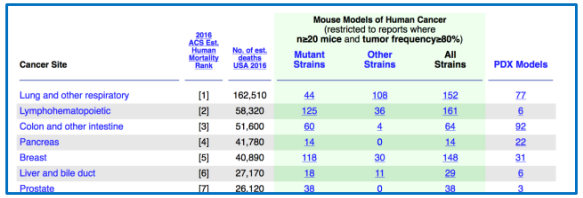


IMPC International Mouse Phenotyping Consortium

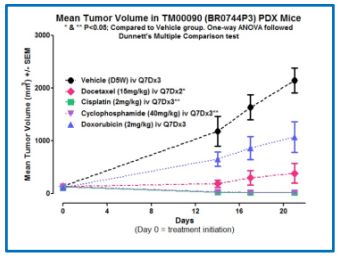
mousephenotype.org



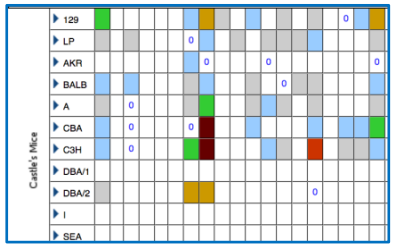
Search



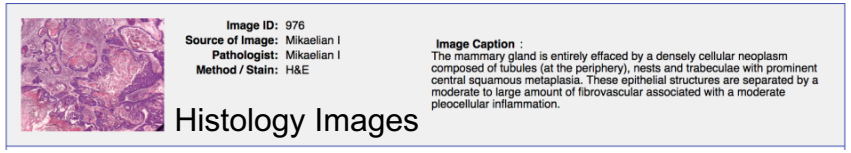
Summaries Of Cancer Mouse lines



Supporting Data



Strains with Cancer Freq.



Histology Images

MTB Mouse Tumor Biology Database

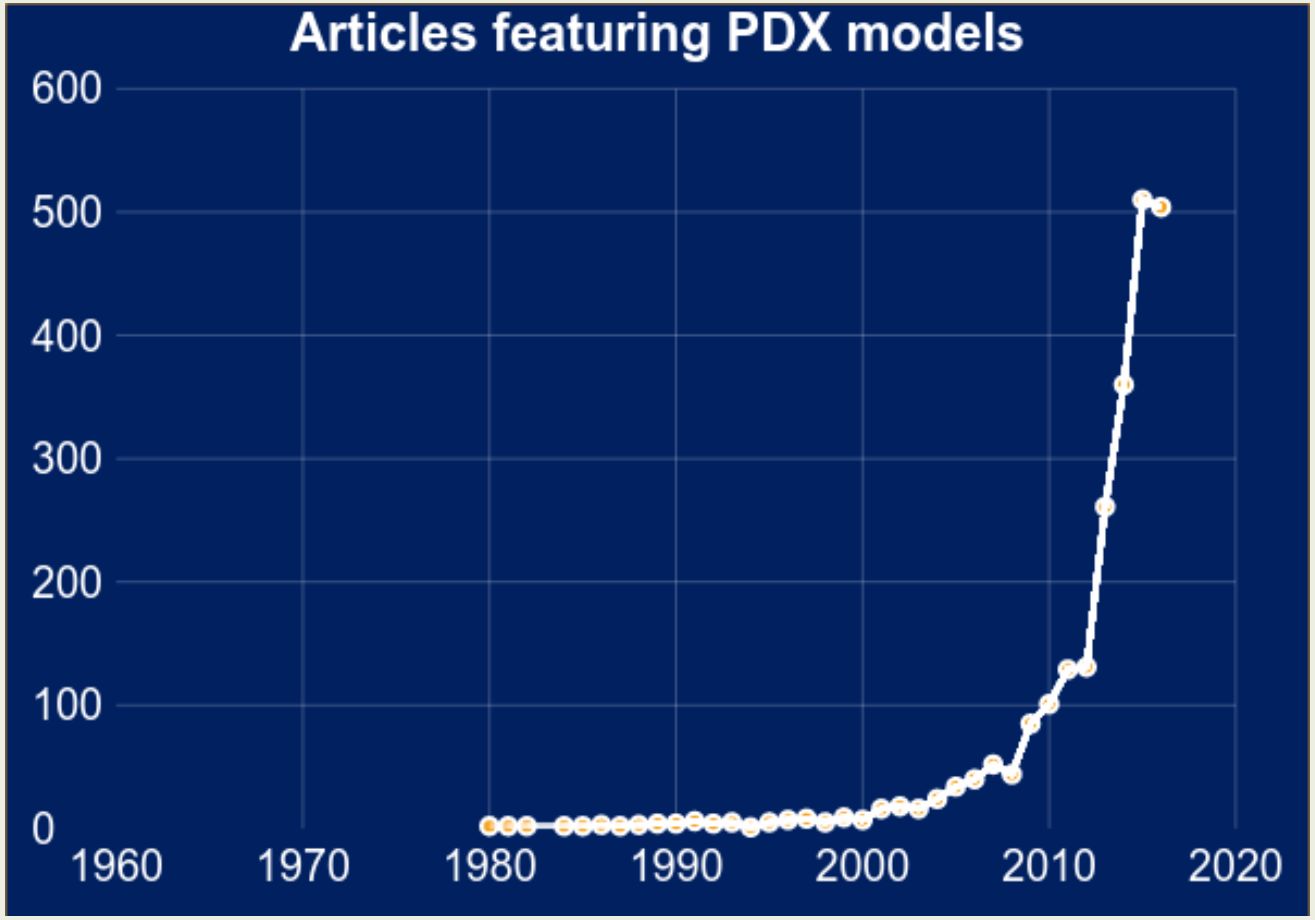
tumor.informatics.jax.org

AIMS

- Allow clinicians and researchers to find relevant PDX models *available for distribution*

- Allow clinicians and researchers to *find and reuse data* from relevant PDX models

PDX MODELS ARE BEING INCREASINGLY USED



Clinical Cancer Research March 2010

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Cancer Therapy: Preclinical

Patient-Derived First Generation Xenografts of Non–Small Cell Lung Cancers: Promising Tools for Predicting Drug Responses for Personalized Chemotherapy

Xin Dong, Jun Guan, John C. English, Julia Flint, John Yee, Kenneth Evans, Nevin Murray, Calum MacAulay, Raymond T. Ng, Peter W. Gout, Wan L. Lam, Janessa Laskin, Victor Ling, Stephen Lam, and Yuzhuo Wang

DOI: 10.1158/1078-0432.CCR-09-2878 Published March 2010

CANCER DISCOVERY Nov 2011

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Research Articles

A Molecularly Annotated Platform of Patient-Derived Xenografts ("Xenopatients") Identifies HER2 as an Effective Therapeutic Target in Cetuximab-Resistant Colorectal Cancer

Feb 2016

US cancer institute to overhaul tumour cell lines

Veteran cells to be retired in favour of fresh tumour samples grown in mice.

Heidi Ledford

Nature News

DEFINING MINIMAL INFORMATION FOR PDX MODELS

- Minimal information standards
- Collaborated with groups interested in PDX data

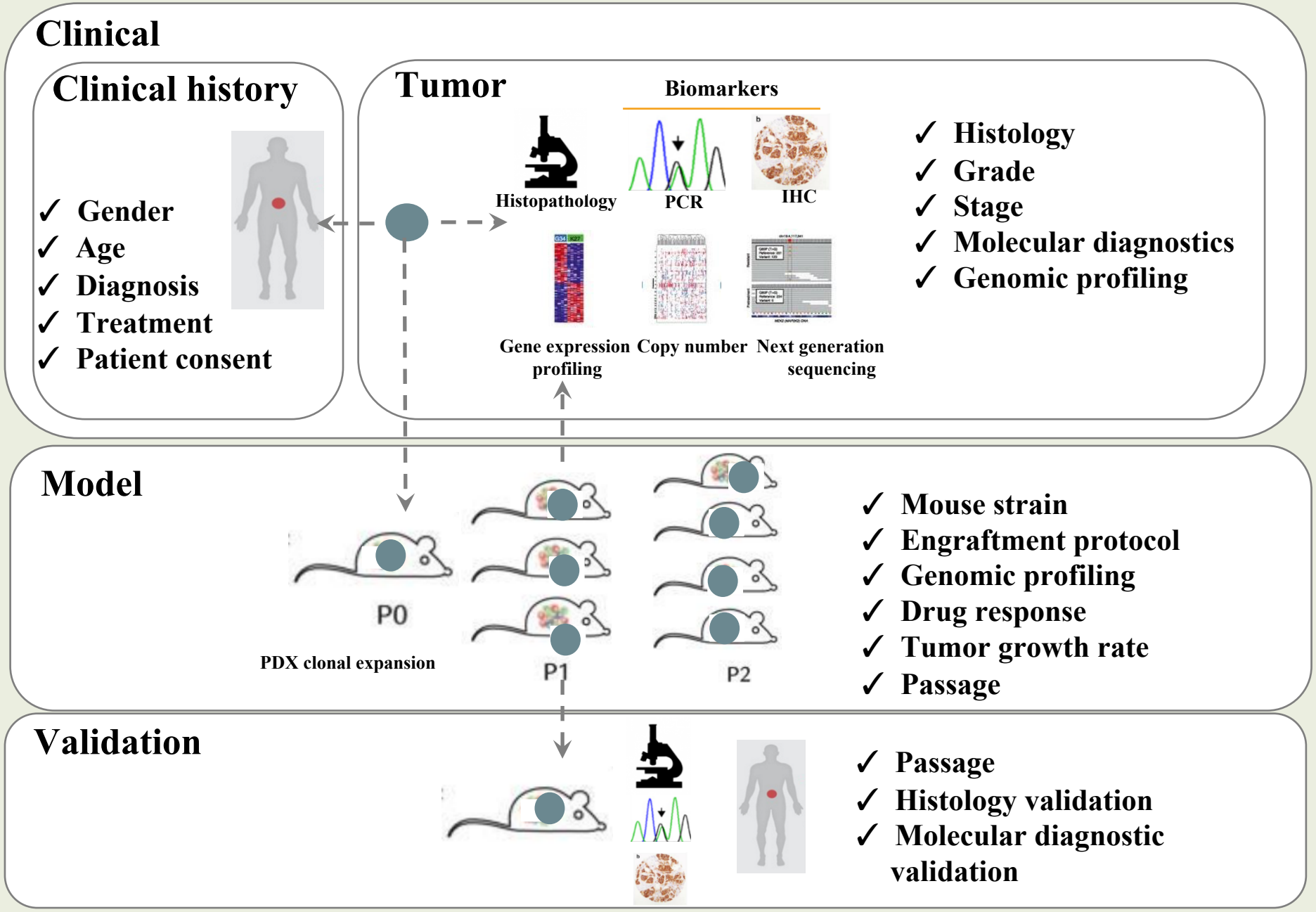
Carol Bult, PhD
Head of MGI, Jackson Laboratory
Scientific Director
PDX and Cancer Avatar program

Atul Butte, MD, PhD
Ted Goldstein, PhD
UCSF Institute for
Computational Health Sciences

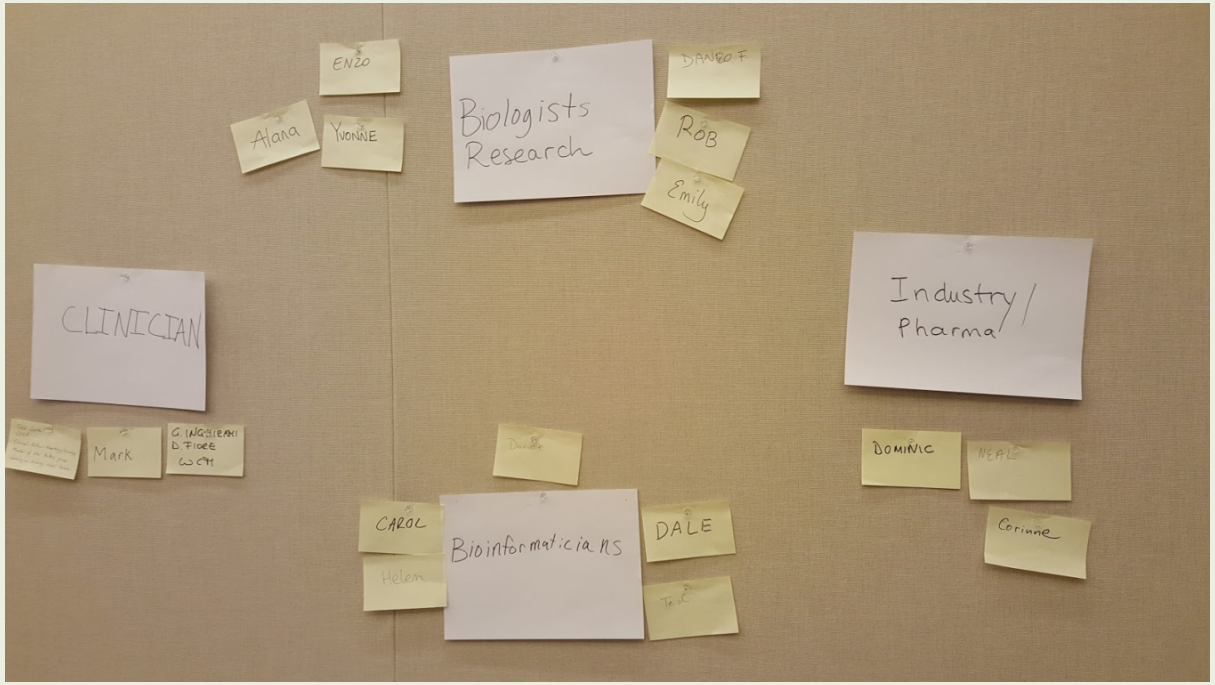
PDX-MI MANUSCRIPT

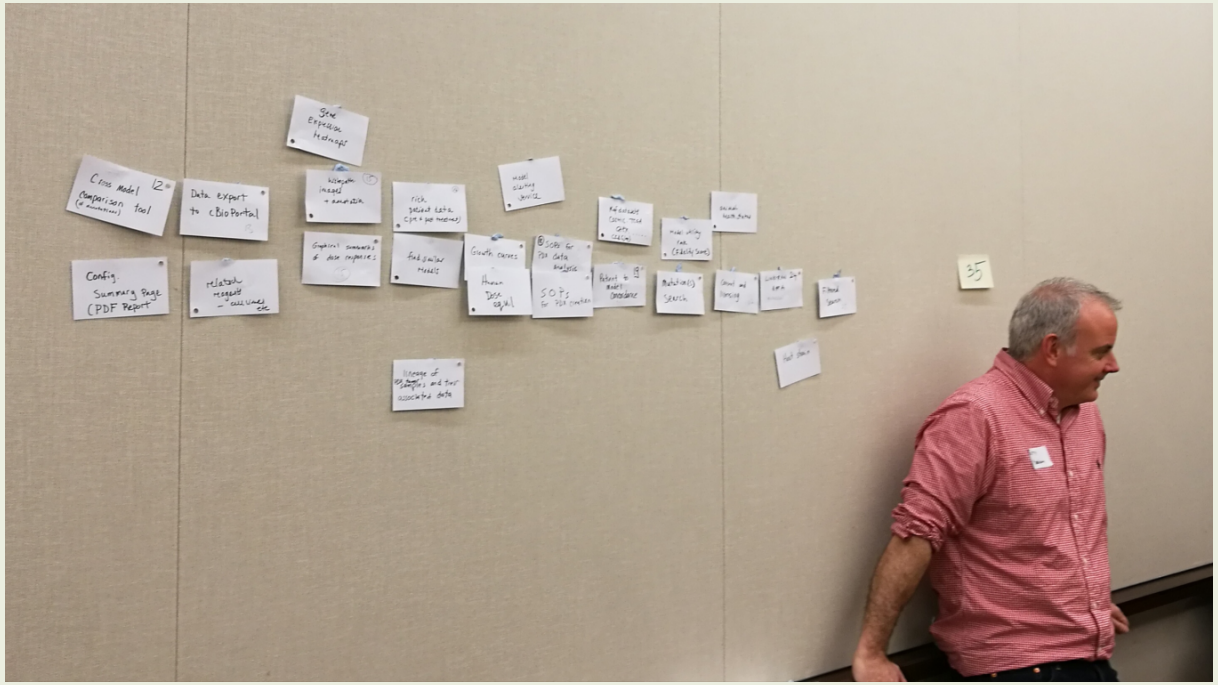
Module	Field	Recommendation	Example entry or choice
Clinical/Patient	Submitter Patient ID	Essential	PAT-125
	Gender	Essential	female
	Age	Essential	50-55 (binned in 5 year age groups)
	Diagnosis	Essential	invasive breast cancer
	Consent to share data	Essential	yes/no/available to academic centers only
	Ethnicity/Race	Desirable	caucasian
	Current Treatment drug	Desirable	everolimus: CHEMBL65
	Current Treatment protocol (dose: details)	Desirable	afinitor:10 mg/day
	Prior treatment protocol	Desirable	surgery and nolvadex: 40 mg/day
	Response to prior treatment	Desirable	progressive disease (RECIST1.1)
	Virology status	Desirable	HIV-/HBV-/HCV+/HTLV-/EBV+
Clinical/Tumor	Submitter Tumor ID	Essential	TUM-125
	Tumor tissue of origin	Essential	liver
	Primary, metastasis, Recurrence	Essential	metastasis
	Tissue histology	Essential	invasive ductal carcinoma
	Tumor Grade: classification	Essential	grade 5: Elston
	Disease Stage: classification	Essential	TSNM1: TNM or Non applicable (example blood cancer)
	Specific markers (diagnostic linked): platform	Essential	ER+, PR+, HER2+: IHC
	Is tumor from untreated patient?	Essential	yes/no
	Original tumor sample type	Desirable	biopsy, surgical sample, ascites fluid, blood, etc
	Tumor from an existing PDX model? ID? why sub-line?	Desirable	Yes, PDX#125, lost cisplatin resistance
Model Creation	Submitter PDX ID	Essential	PDX#125
	Mouse strain (and source)	Essential	NOD.Cg-Prkdc<scid>Il2rg<tm1Wjl>/SzJ, The Jackson Laboratory
	Strain immune system humanized?	Essential	yes/no
	Type of humanisation	Essential	CD34+ hematopoietic stem cell-engrafted/ PBMC/ Thymus/ Thymus-fetal liver/ iPSC/other
	Tumor preparation	Essential	tumor solid, cell suspension, ascite
	Injection type and site	Essential	subcutaneous: right flank
	Mouse treatment for engraftment	Desirable	estrogen treatment
	Engraftment rate	Desirable	50%
	Engraftment time	Desirable	5 weeks
Model Quality Assurance	Tumor Characterization Technology	Essential	histology and IHC
	Tumor confirmed not to be of mouse/EBV origin	Essential	yes/no: negative for murine CD45
	Response to Standard of Care (Pharmacological positive control)	Desirable	Not assessed / Assessed- complete response, partial response, stable disease, progressive disease
	Animal health status	Desirable	SPF/SOPF, C.Bovis & Pneumocystis negative/positive
	Passage QA performed	Essential	passage P4
Model study	Treatment, passage	Desirable	pertuzumab in combination with trastuzumab: CHEMBL2037641 and CHEMBL1745062: passage P4
	Treatment protocol (dose: details)	Desirable	trastuzumab (50 mg/kg loading dose, 15 mg/kg weekly); pertuzumab (50 mg/kg loading dose, 15 mg/kg weekly)
	Treatment Response	Desirable	complete response, partial response, stable disease, progressive disease
	Tumor DMICS: sample id: sample site: purity (mouse vs human): technology: passage	Desirable	TUMpdx-125: subcutaneous: 90% human: exome sequencing: passage P5
	Development of metastases in strain (Y/N, site): passage	Desirable	Yes: liver: passage P8
	Lag time/doubling time of tumor	Desirable	48h
Associated metadata	PDX model availability ?	Desirable	yes/no: frozen tumour: live mouse
	governance restriction for distribution	Desirable	available to academic centers only
	ID for associated publication, image, archived data (URL, PMID, DOI)	Desirable	http://www.dataset.org/EXA125: PMID:25025745: DOI: 10.1186/s13059-015-0525-1

- Feedback from over 35 institutes
  - Pharmaceutical
  - Clinical Research groups
  - Academic labs
- Final Revision dedicated informatics issue of *Cancer Research*


Clinical
Clinical history
✓ Gender
✓ Age
✓ Diagnosis
✓ Treatment
✓ Patient consent
Tumor
Biomarkers
Histopathology
PCR
IHC
Gene expression profiling
Copy number
Next generation sequencing
✓ Histology
✓ Grade
✓ Stage
✓ Molecular diagnostics
✓ Genomic profiling
Model
P0
PDX clonal expansion
P1
P2
✓ Mouse strain
✓ Engraftment protocol
✓ Genomic profiling
✓ Drug response
✓ Tumor growth rate
✓ Passage
Validation
✓ Passage
✓ Histology validation
✓ Molecular diagnostic validation

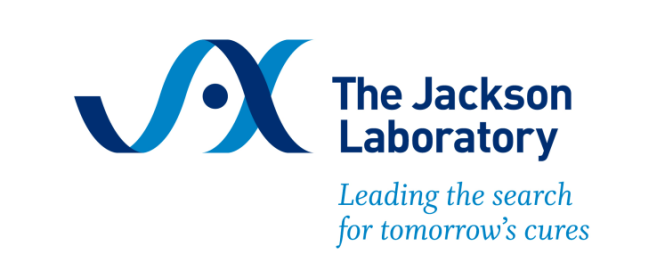
2017 AACR SATELLITE MEETING
PDX USER REQUIREMENTS WORKSHOP





- 25 participants
- Interactive workshop with 25 experts

PDX FINDER
JAX AND EBI CO-DEVELOPED RESOURCE



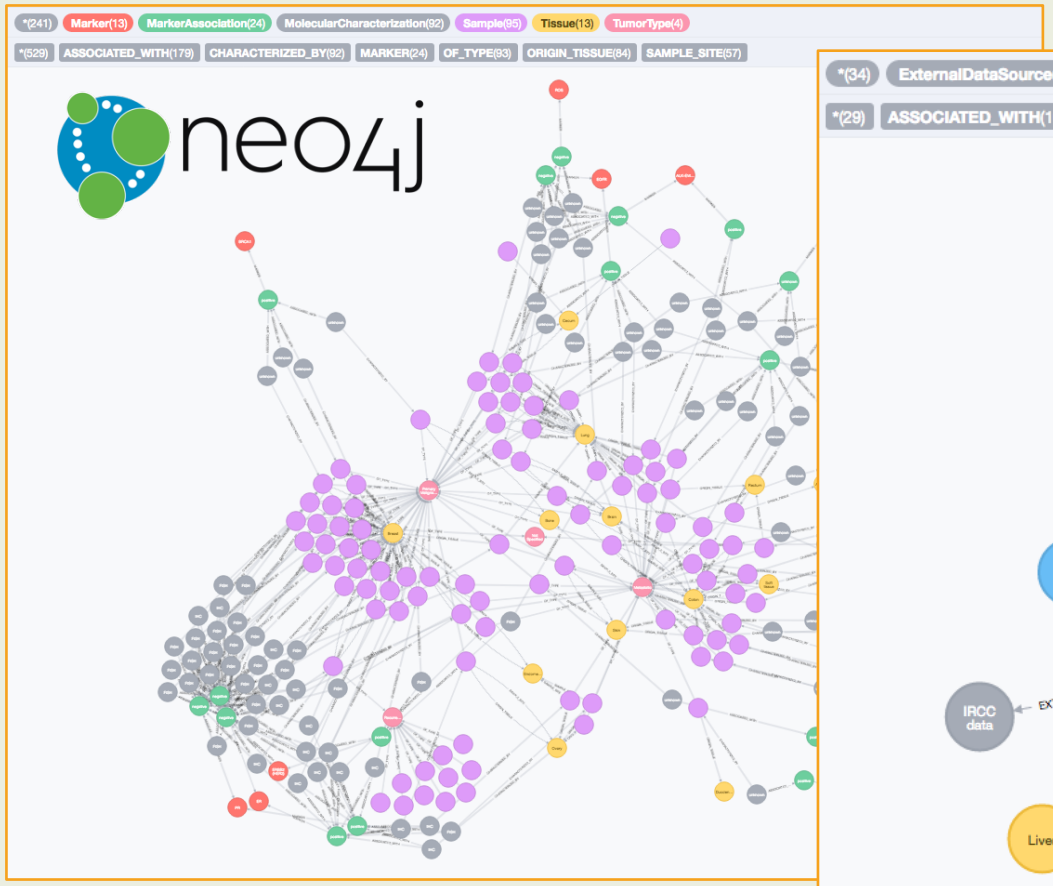
400 models from common cancers

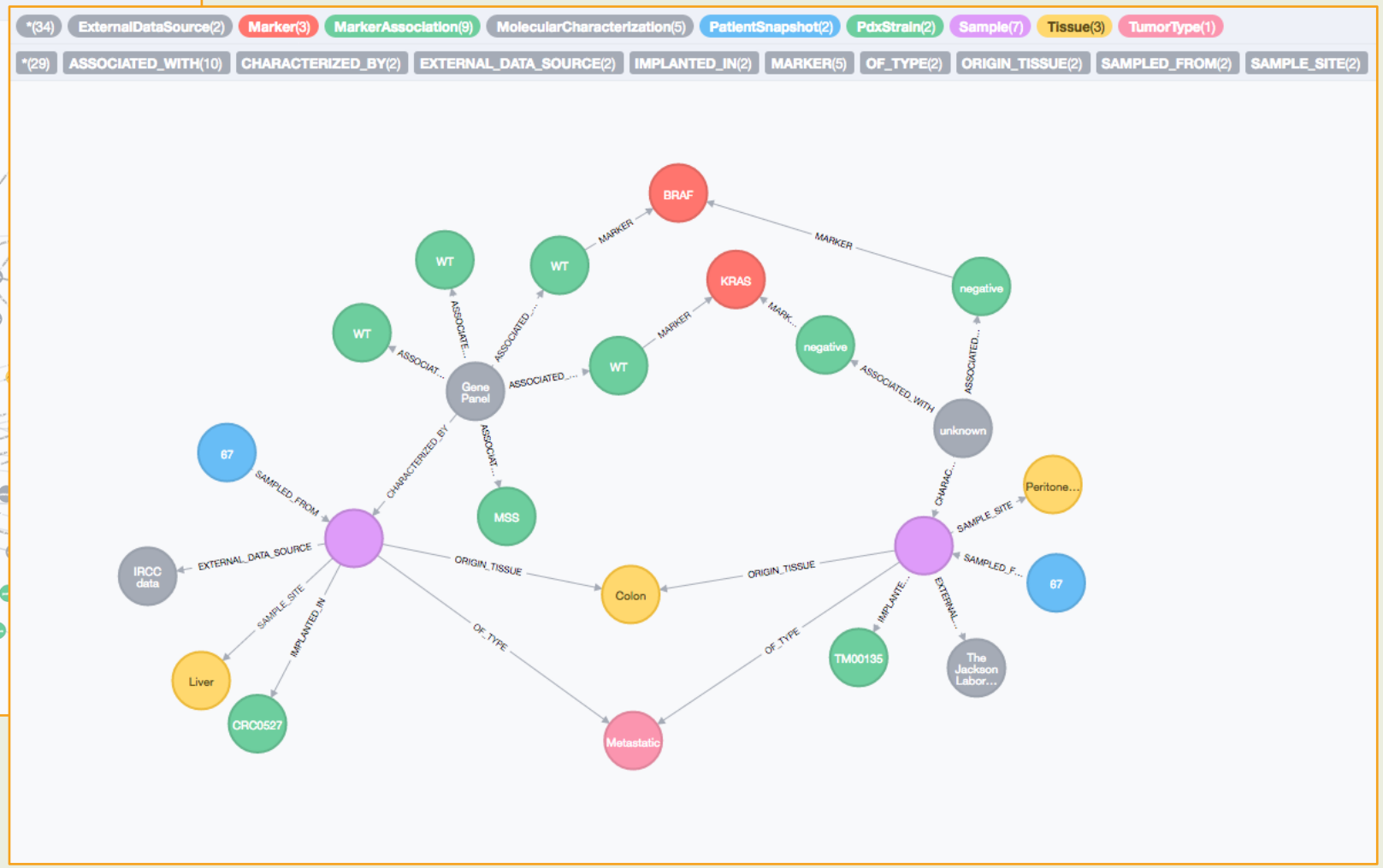
www.pdxfinder.org

400 colorectal Adenocarcinoma models from IRCC Univ. of Turin

UCSF School of Medicine

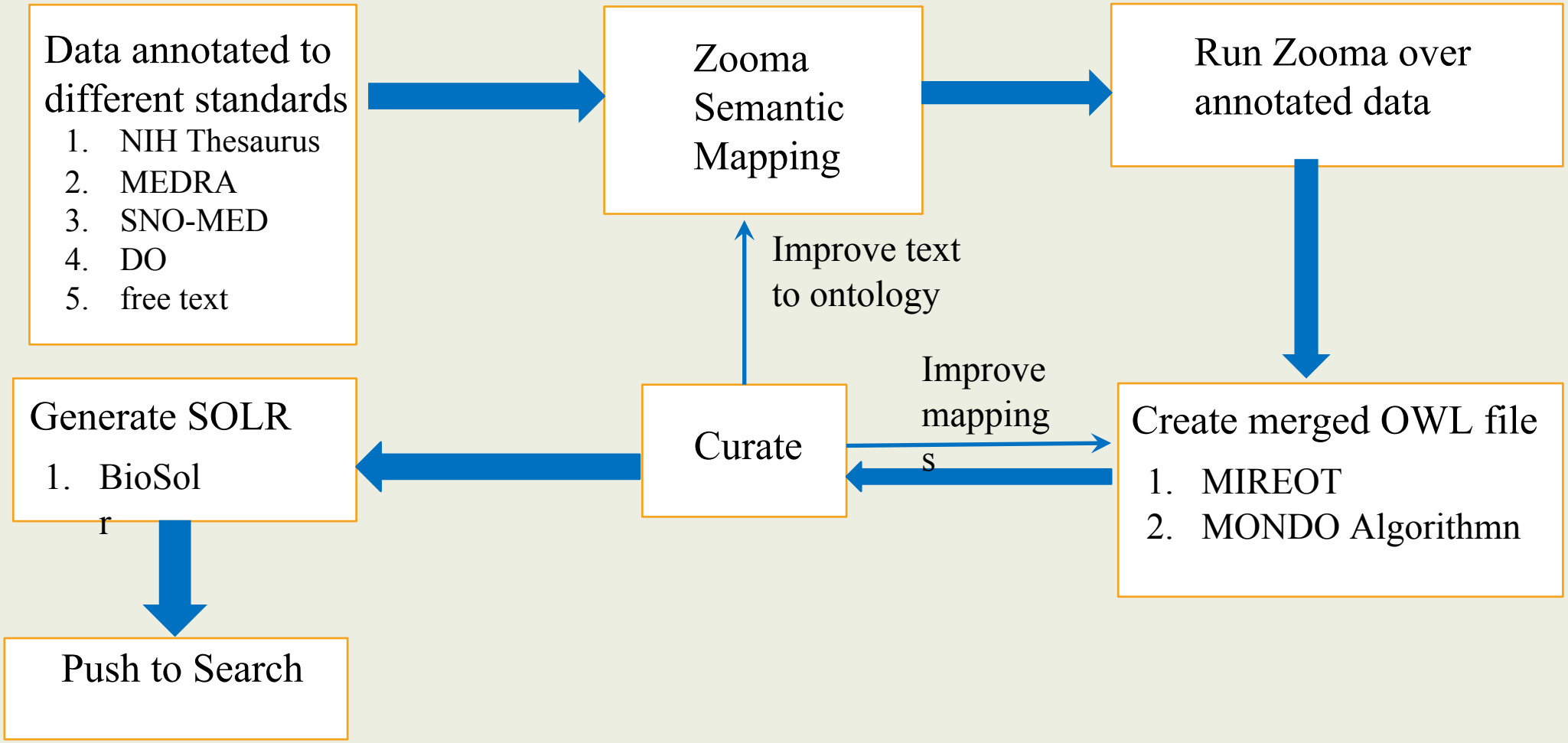
PDX FINDER
A GRAPH DATABASE BACKEND





github.com/pdxfinder

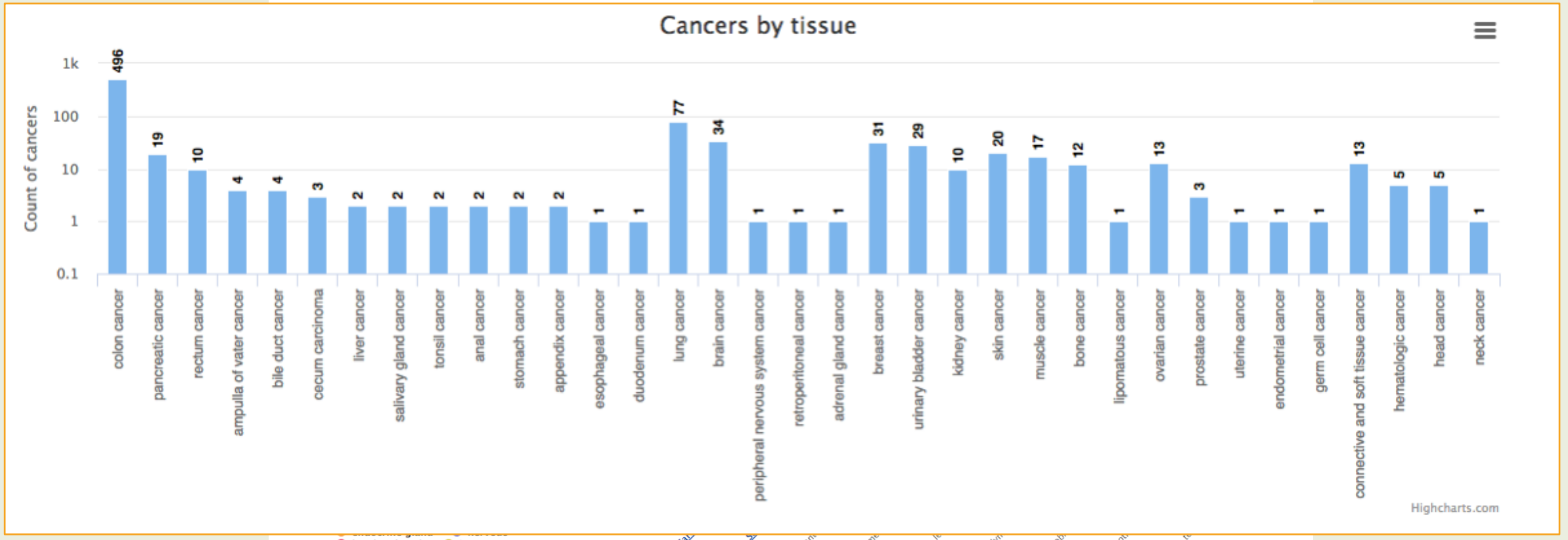
PDX FINDER
A SEMANTIC MIDDLE LAYER



PDX FINDER
PROTOTYPE FRONT END

Patient Derived Xenograft Finder

www.pdxfinder.or



head and neck
intergumentary
urinary
musculoskeletal
reproductive organ
respiratory
breast

Highcharts.com

Highcharts.com

PDX FINDER
MODEL SUMMARY PAGE

JAXPT1554

Clinical / Patient

Patient ID	JAXPT1554
Gender	Female
Age	56
Race	White
Ethnicity	Not Reported

Clinical / Tumor

Diagnosis	adenocarcinoma
Tumor type	Metastatic
Classification	IV/
Markers	BRAF status: negative, KRAS status: negative

PDX model creation

Sample type	
Strain	
Mouse sex	
Engraftment site	

PDX model studies

Coming soon...

View data at JAX

LEVERAGING RESOURCES AT EMBL-EBI

Genes, genomes & variation

- European Nucleotide Archive
- European Variation Archive
- European Genome-phenome Archive
- Ensembl
- Ensembl Genomes
- GWAS Catalog
- Metagenomics portal

Gene, protein & metabolite expression

- RNA Central ArrayExpress
- Expression Atlas
- Metabolights
- PRIDE

Protein sequences, families & motifs

- InterPro
- Pfam
- UniProt

Molecular structures

- Protein Data Bank in Europe
- Electron Microscopy Data Bank

Chemical biology

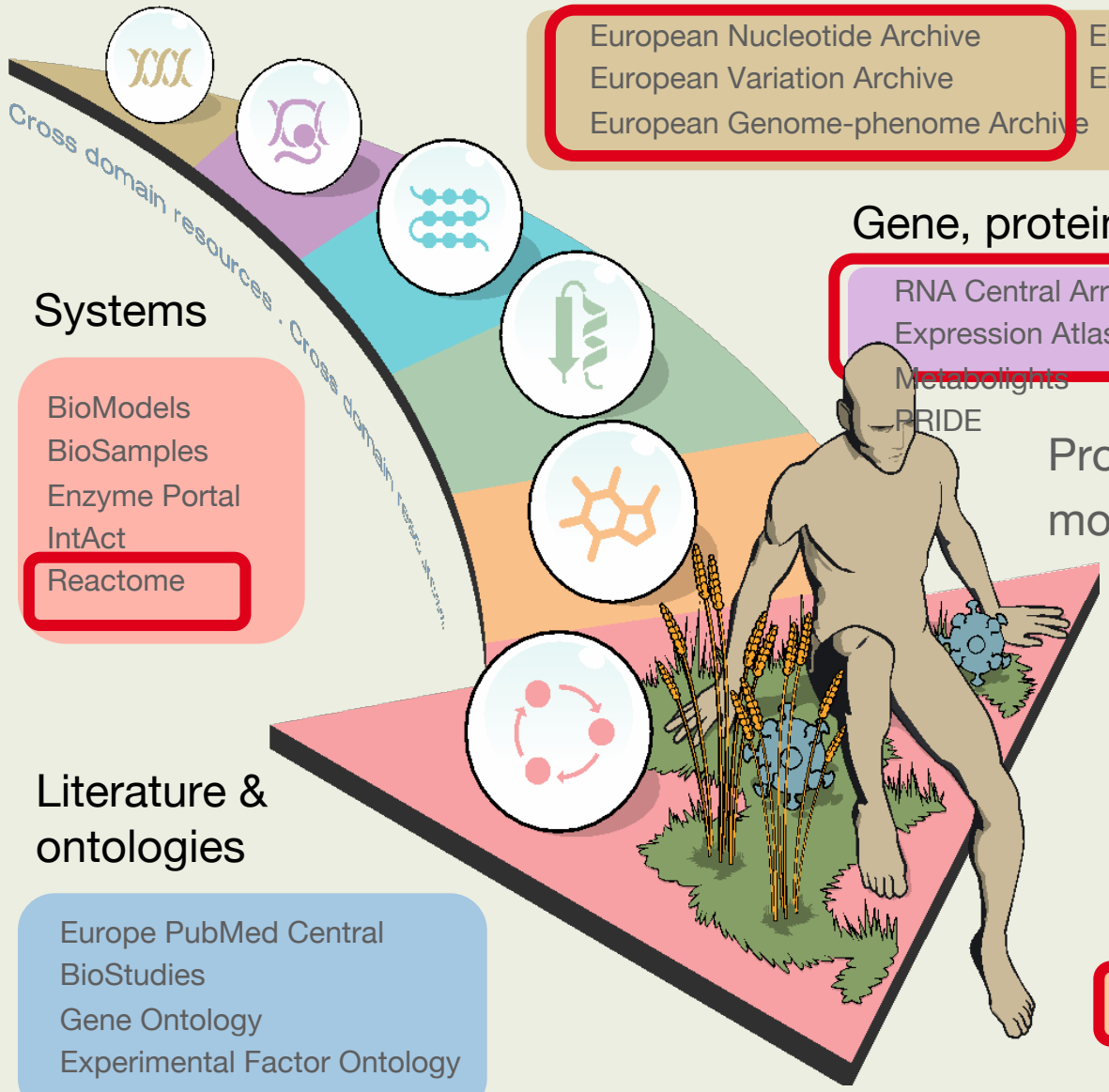
- ChEMBL
- SureChEMBL
- ChEBI

Systems

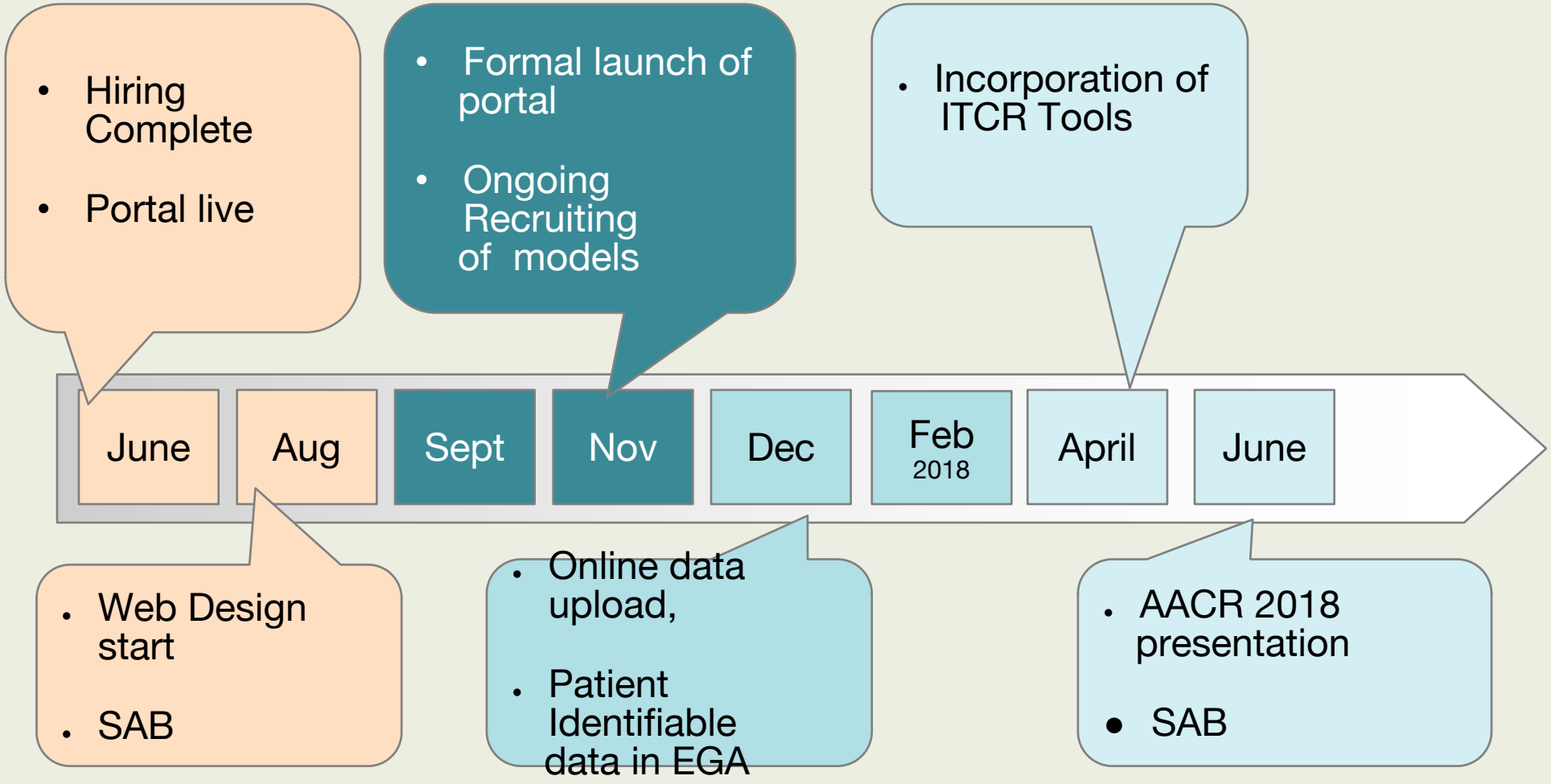
- BioModels
- BioSamples
- Enzyme Portal
- IntAct
- Reactome

Literature & ontologies

- Europe PubMed Central
- BioStudies
- Gene Ontology
- Experimental Factor Ontology



ONE YEAR TIMELINE



PDX models to register in the next year:

- PDM Repository
- International Breast Cancer Consortium
- PROXE
- EuroPDX
- German Pediatric Brain Tumors

ACKNOWLEDGEMENTS

The Jackson Laboratory

- Carol Bult
- Steven Neuhauser
- Dale Begley
- Debbie Krupke

EMBL-EBI

- Helen Parkinson
- Nathalie Conte
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- Abayomi Mosaku
- Minjie Ding (EGA)

UCSF School of Medicine

- Atul Butte
- Ted Goldstein (UCSC)
- Zhiping Gu (NGC)
- Jeffrey A Wiser (NGC)
- Patrick Dunn, (NIH/NIAID)

www.PDXfinder.org
Contact us: helpdesk@pdxfinder.org

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PDM

EurOPDX
Translating Knowledge in Oncology

QUESTIONS