CrownBio
CONNECTING SCIENCE TO PATIENTS

Corporate Headquarters:
16550 West Bernardo Drive
Building 5, Suite 525
San Diego, CA 92127
Tel: 855.827.6968
Fax: 888.882.4881
www.crownbio.com

Leveraging 3D *In Vitro M*odels for Oncology Drug Discovery

Rajendra Kumari, PhD
Global Head of Scientific Communications

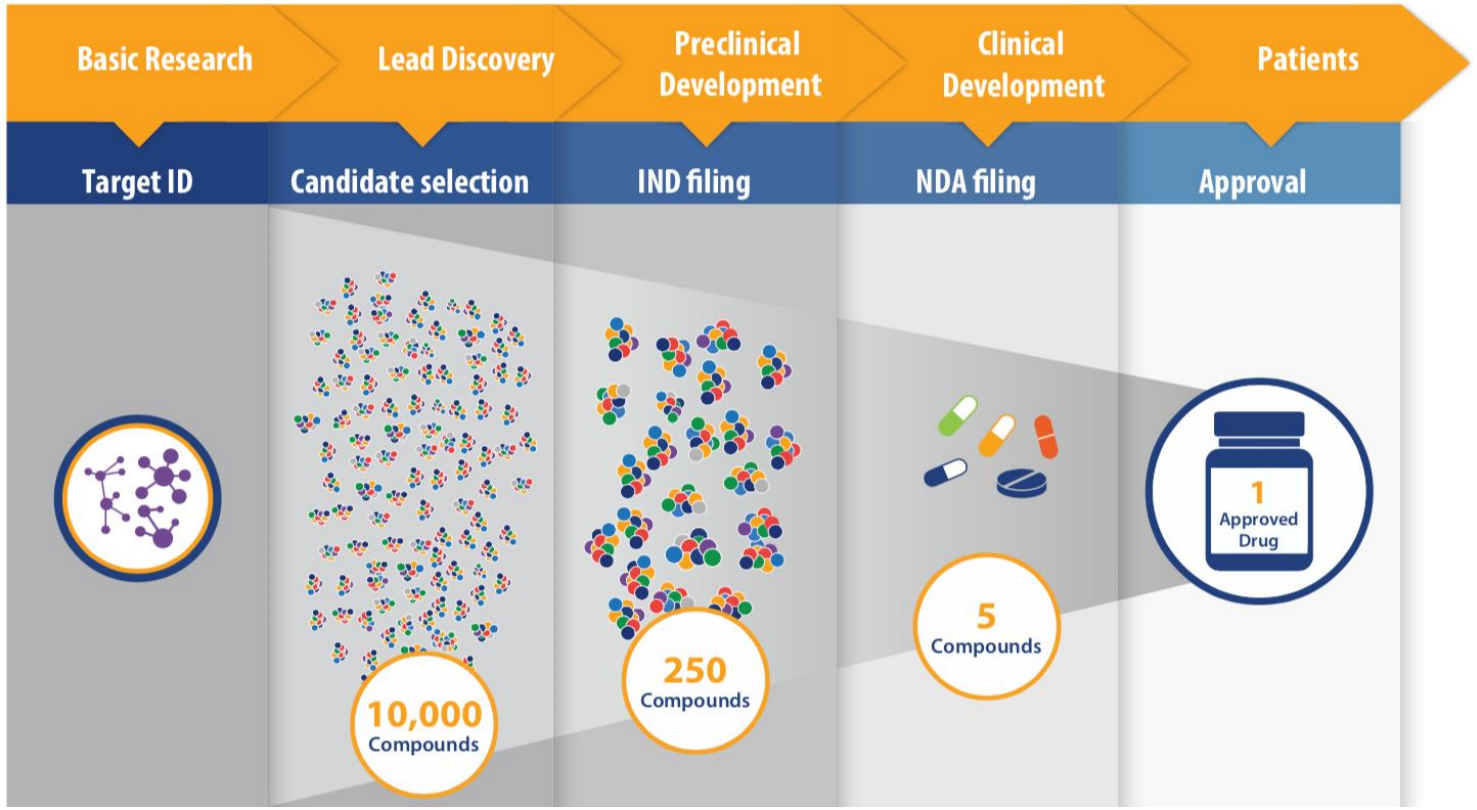
Speaker
Rajendra Kumari, PhD

- Received her PhD from the University of Leicester in Molecular Pharmacology, followed by postdoctoral fellowships in the Division of Preclinical Oncology, University of Nottingham, and lectureship in the School of Clinical Sciences
- Co-founder of PRECOS Ltd in 2010, a spin-out company providing preclinical oncology services for *in vitro* and *in vivo* research, as well as imaging, taking the role of Chief Operations Officer
- PRECOS merged with CrownBio in 2013, where Rajendra served as General Manager and Chief Scientific Officer of CrownBio's European facility in the UK
- Currently is the Global Head of Scientific Communication
- Rajendra is a member of the American Association of Cancer Research and the British Association of Cancer Research, and has authored over 40 abstracts and publications

Webinar Overview

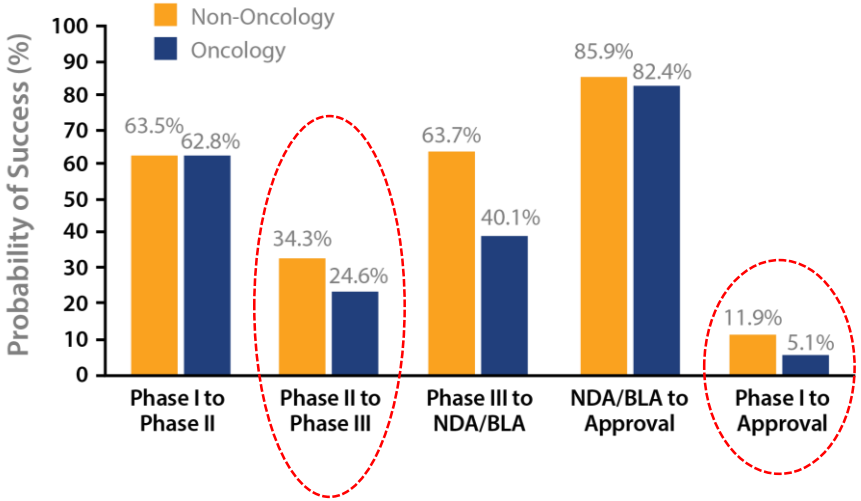
- Bridging the gap between the lab and the clinic
- Key advantages of using 3D *in vitro* systems
- When to use 3D *in vitro* platforms, including new technology like organoids
- How to integrate organoids into your drug discovery program and when to look for alternatives
- Predicting *in vivo* responses to move forward with

Current Linear Drug Discovery Process: Inefficient, Costly and Risky



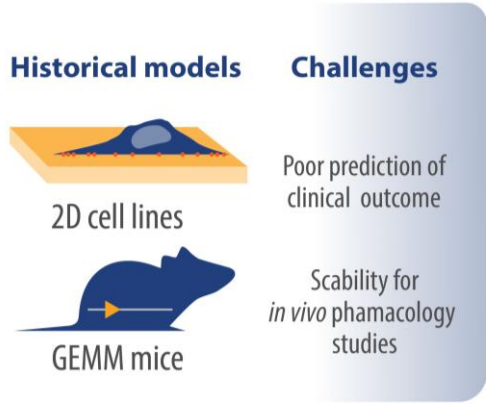
Cancer drug development

- Most candidates fail
- Attrition rates particularly high

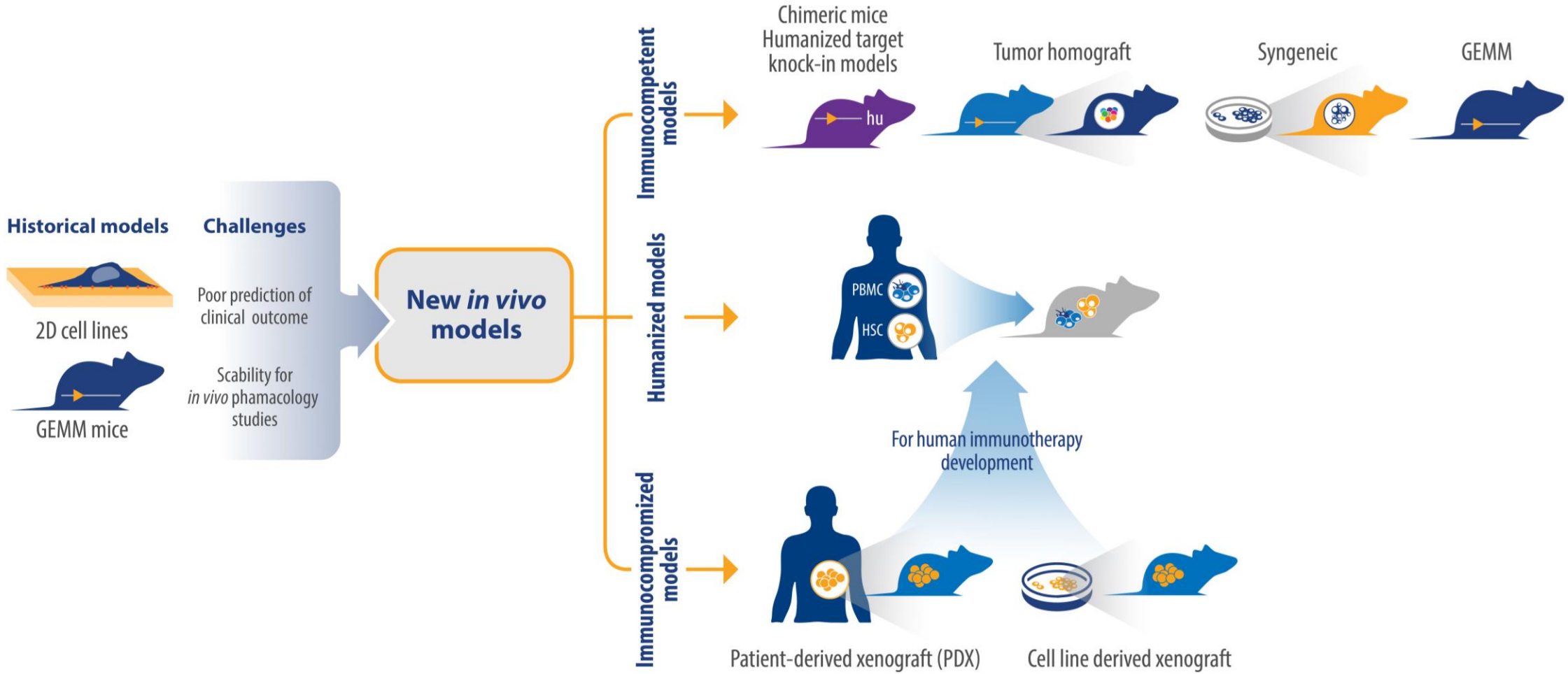


Nat Rev Drug Discov, 2004, 3:711

Preclinical Tumor Models for Oncology Drug Discovery



Preclinical Tumor Models for Oncology Drug Discovery



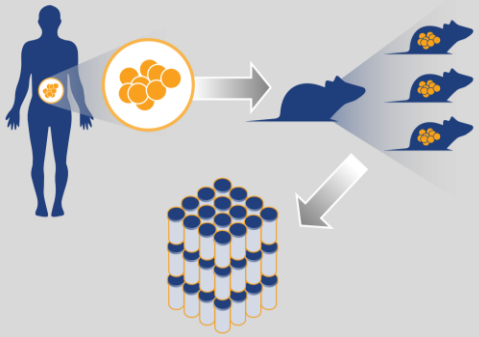
Patient-Derived Models Bridge the Gap Between Lab and Clinic

- Preserve original tumor histo- and molecular pathology
- Recapitulate intra- and inter-patient heterogeneity, and patient diversity
- Pharmacologically predictive

The Value of Patient-Derived Model Biobanks

In Vivo

PDX development and biobanking



Large, diverse, and well characterized biobank

From US, European, and Asian populations

52.0% ASIAN | 47.7% USA/EU | 0.3% OTHERS

30 different cancer types

PDX Mouse Clinical Trial (MCT)

RCT-MCT:"1" or "n+n"
Multiple Indications and Targets

Data analysis
(Paired survival analysis)

HuPrime®

~2500 PDX
established and
~1500 RNASeq'd

HuBase™

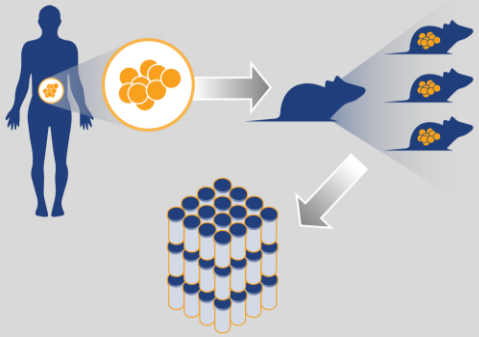
Online searchable PDX database to access genomic annotation

Register at: https://www.crownbio.com/hb-registration

The Value of Patient-Derived Model Biobanks

In Vivo

PDX development and biobanking



Large, diverse, and well characterized biobank

From US, European, and Asian populations

52.0% ASIAN | 47.7% USA/EU | 0.3% OTHERS

30 different cancer types

PDX Mouse Clinical Trial (MCT)

RCT-MCT:"1" or "n+n"
Multiple Indications and Targets

Data analysis
(Paired survival analysis)

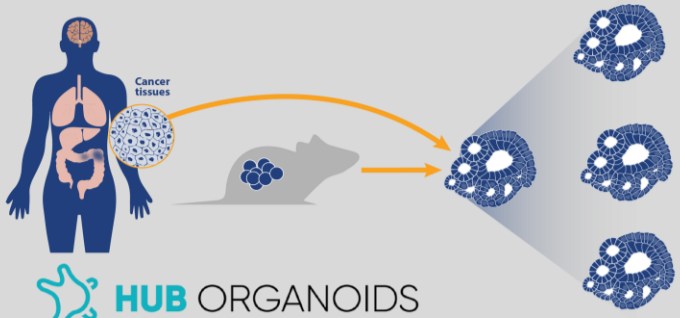
HuPrime®
~2500 PDX
established and
~1500 RNASeq'd

HuBase™
Online searchable PDX database to access genomic annotation

Register at: https://www.crownbio.com/hb-registration

In Vitro 3D

Organoid development and biobanking



HUB ORGANOIDS

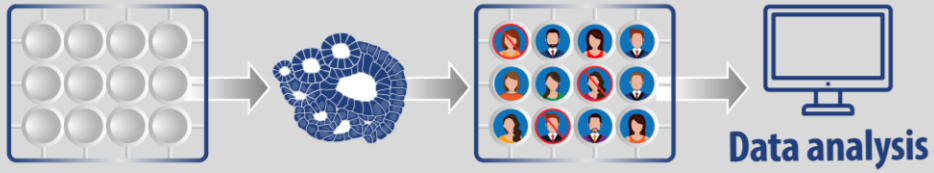
Large, diverse, and well characterized biobank

From Western and Asian populations

50% Western
50% Asian

15 different cancer types

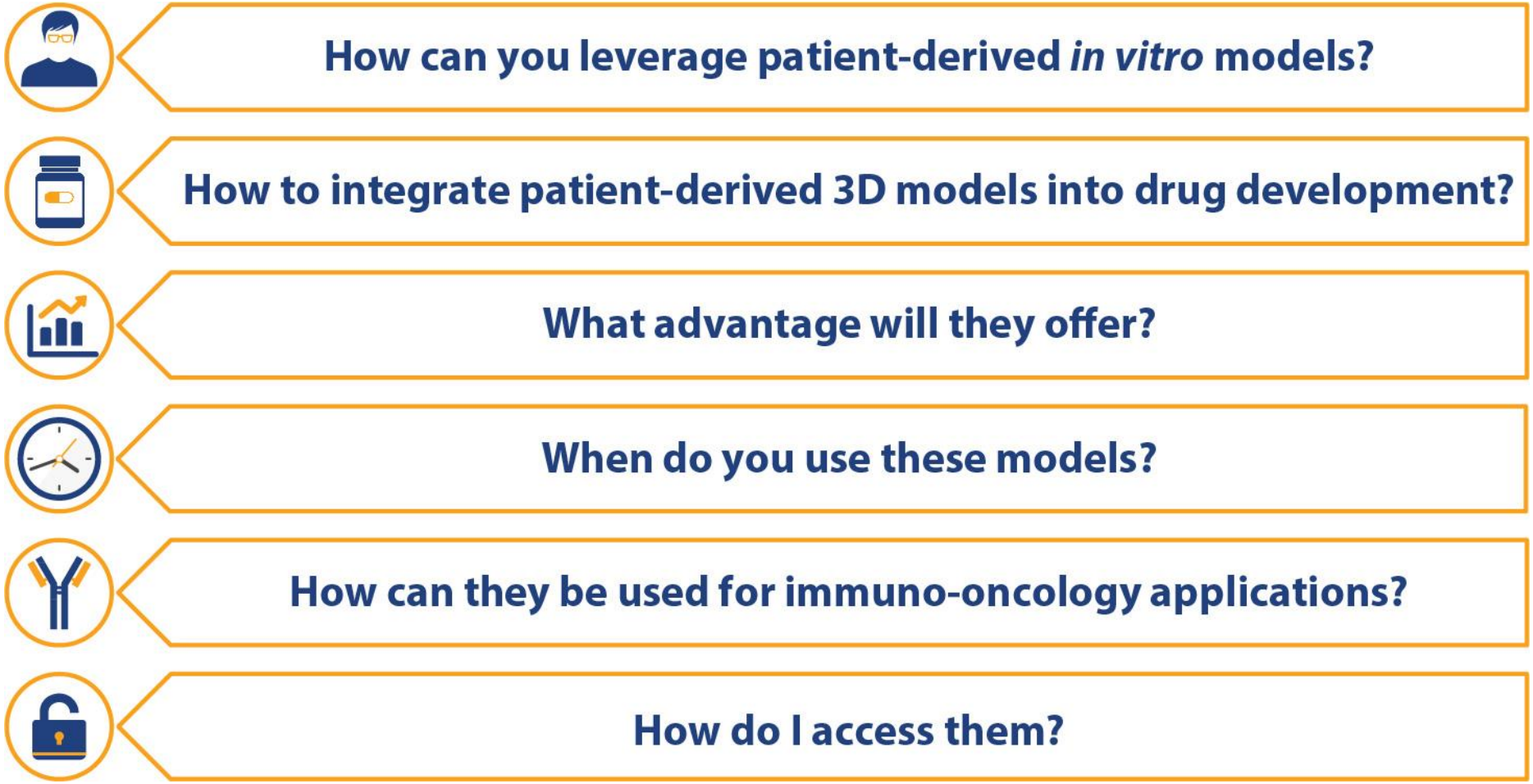
Clinical Trial in a Dish (CTiD)



Data analysis

Register at: https://www.crownbio.com/ob-registration

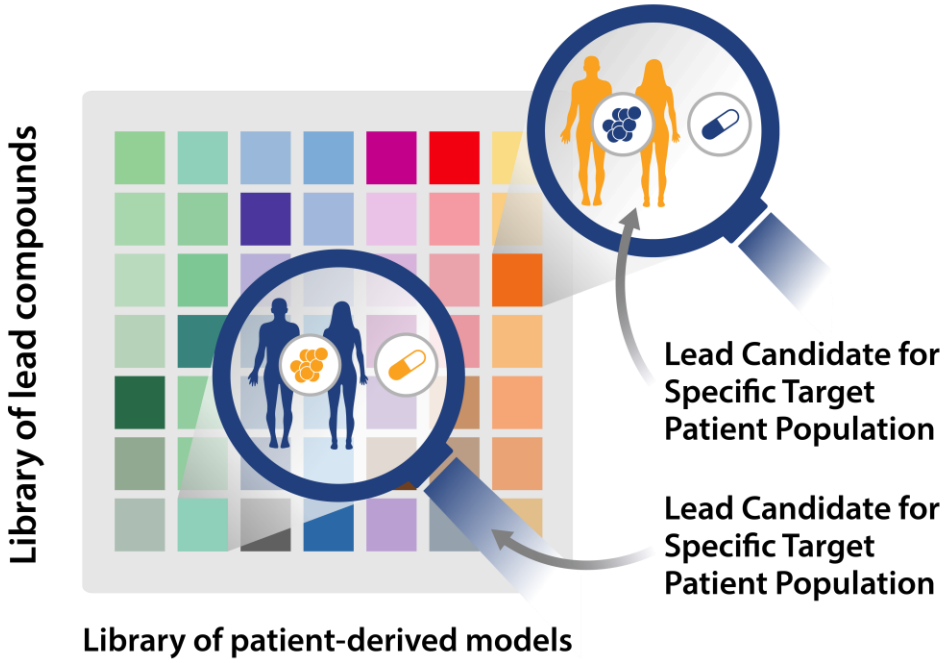
Integration into the Drug Development Process



An Improved Workflow in Oncology Drug Discovery is Needed

- Drug discovery requires selection on **“two variables”**
  - **A lead compound** by screening large numbers of drug candidates
  - **A target patient population** (indication) by screening a diverse portfolio of disease models

- Accelerate and simplify clinical development by screening **lead/model libraries** simultaneously via a **matrix high-throughput screen** (HTS)
- Identify potential **CDx** or **biomarkers** of response
- **Mouse clinical trials** have inherent limitations in handling this type of screening, e.g. time, cost



In Vitro/Ex Vivo Preclinical Tumor Models

2D systems

- Primary cell cultures
- Standard cell lines
- Engineered lines
- Co-incubation

3D systems

- Patient-derived organoids
- *Ex vivo* cell cultures
- Standard cell lines
- Engineered lines
- Co-cultures

Ex vivo tissue

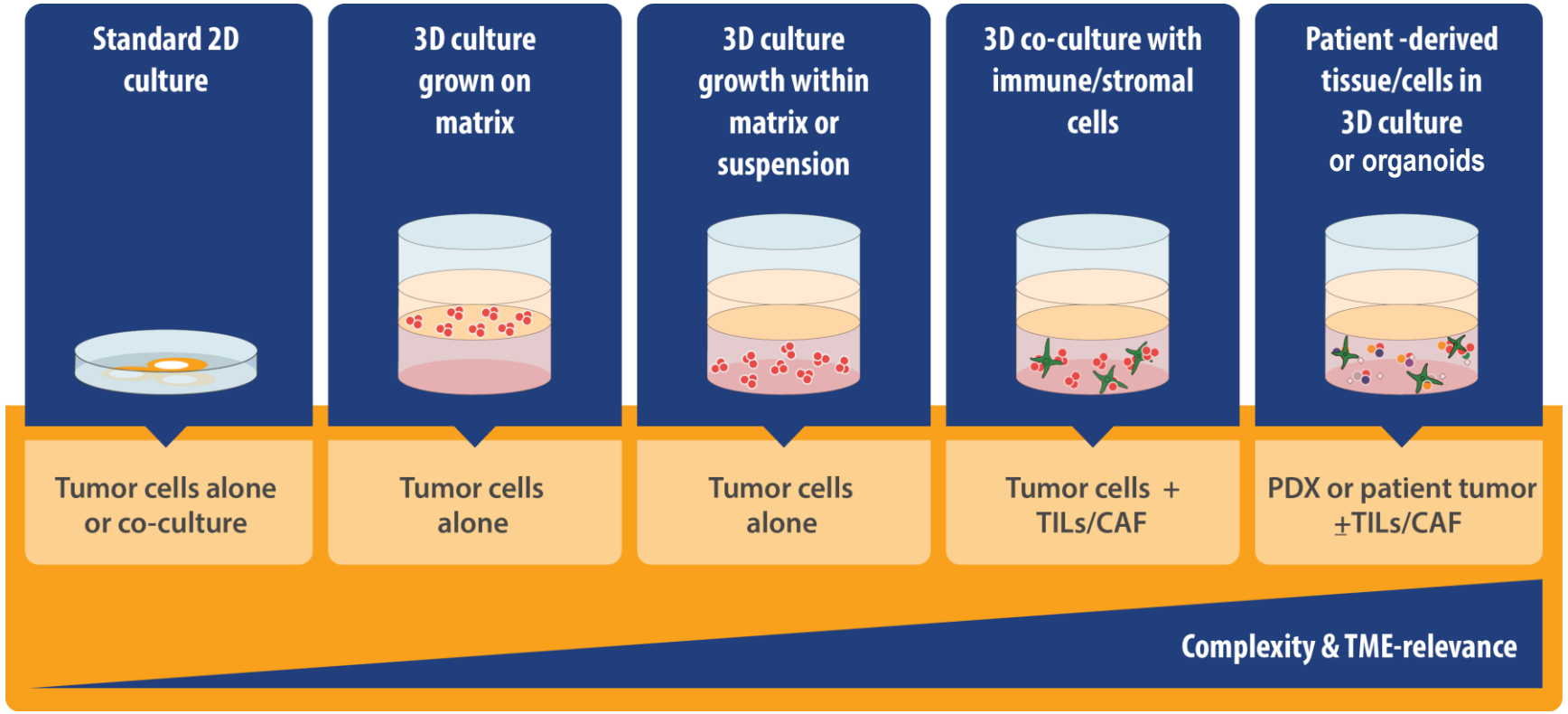
- Patient-derived
- Animal-derived

Navigate Between 2D and 3D Systems

SELECTING IN VITRO SYSTEMS FOR ONCOLOGY DRUG DISCOVERY

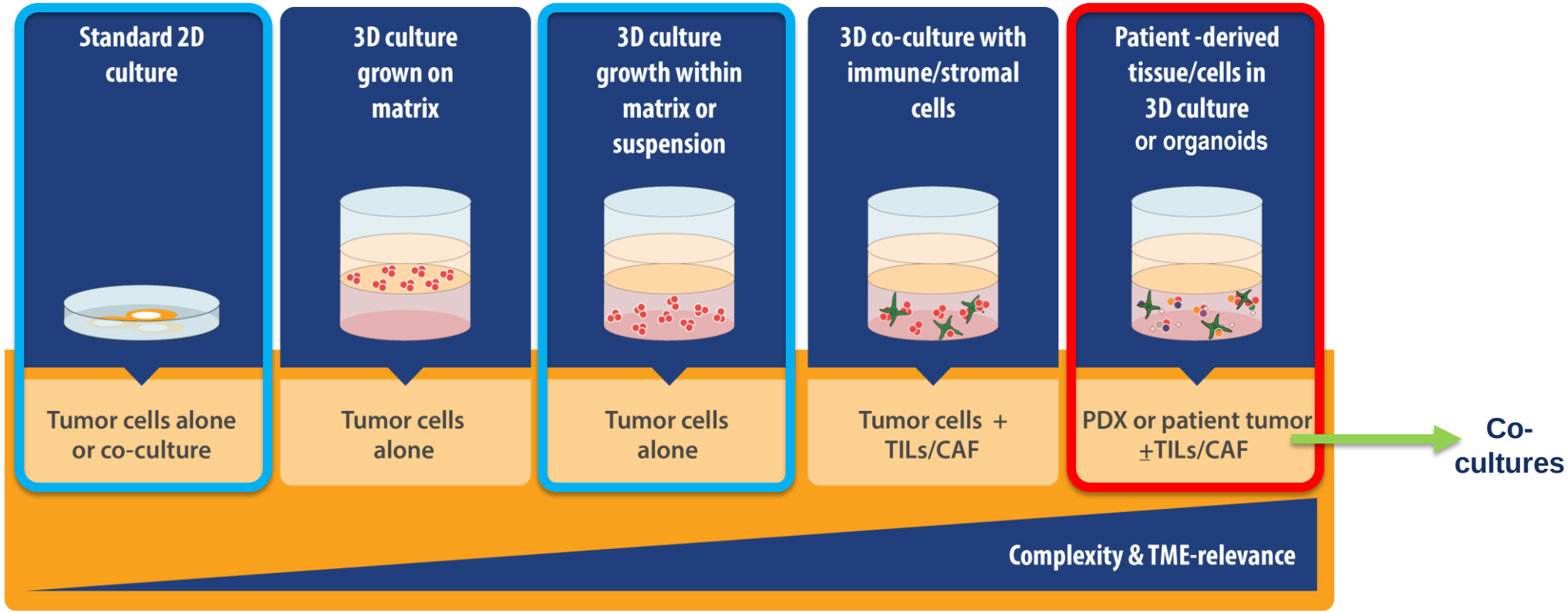
Tumor Microenvironment (TME) Relevance

- 3D modelling increases patient relevance and potentially impacts complexity and throughput



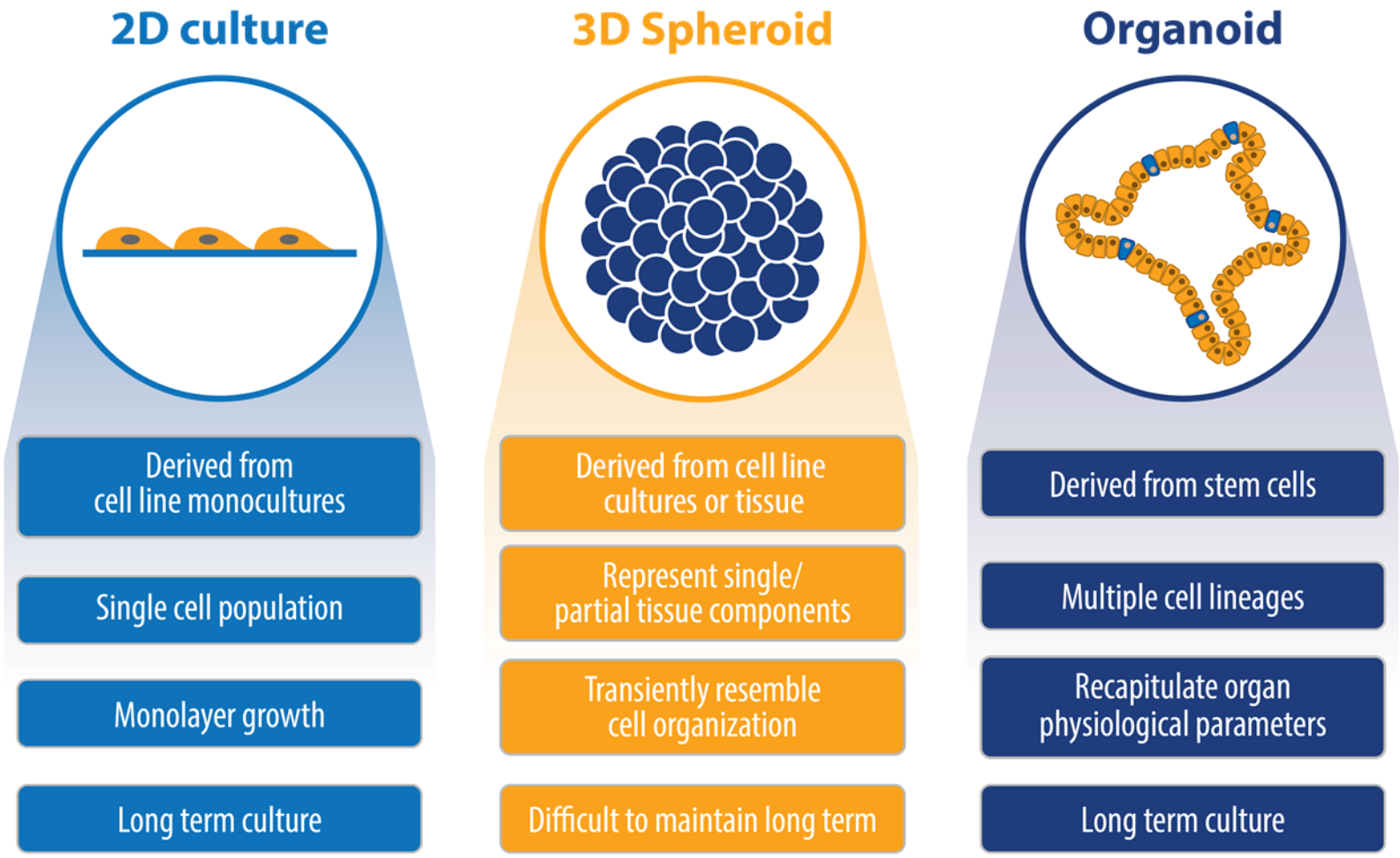
Tumor Microenvironment (TME) Relevance

- 3D modelling increases patient relevance and potentially impacts complexity and throughput

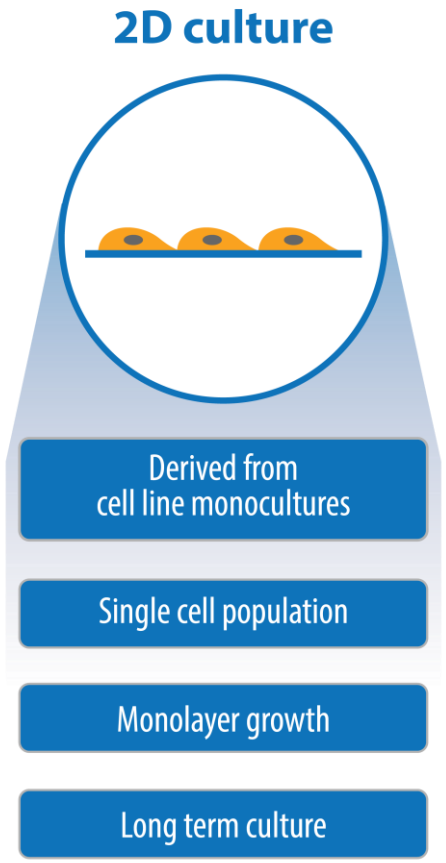


CrownBio
CONNECTING SCIENCE TO PATIENTS

Key Features



Why Use 2D Cell-Based Models?



Advantages

- Robust & reproducible, with high performance & low cost
- Simple and long-term culturing, amenable to engineering
- Large collection of well published models available
- Commercial tests widely available

Limitations

- Poor translatability *in vivo,* as they do not mimic the natural tumor or tissue structure
- Limited heterogeneity and diversity

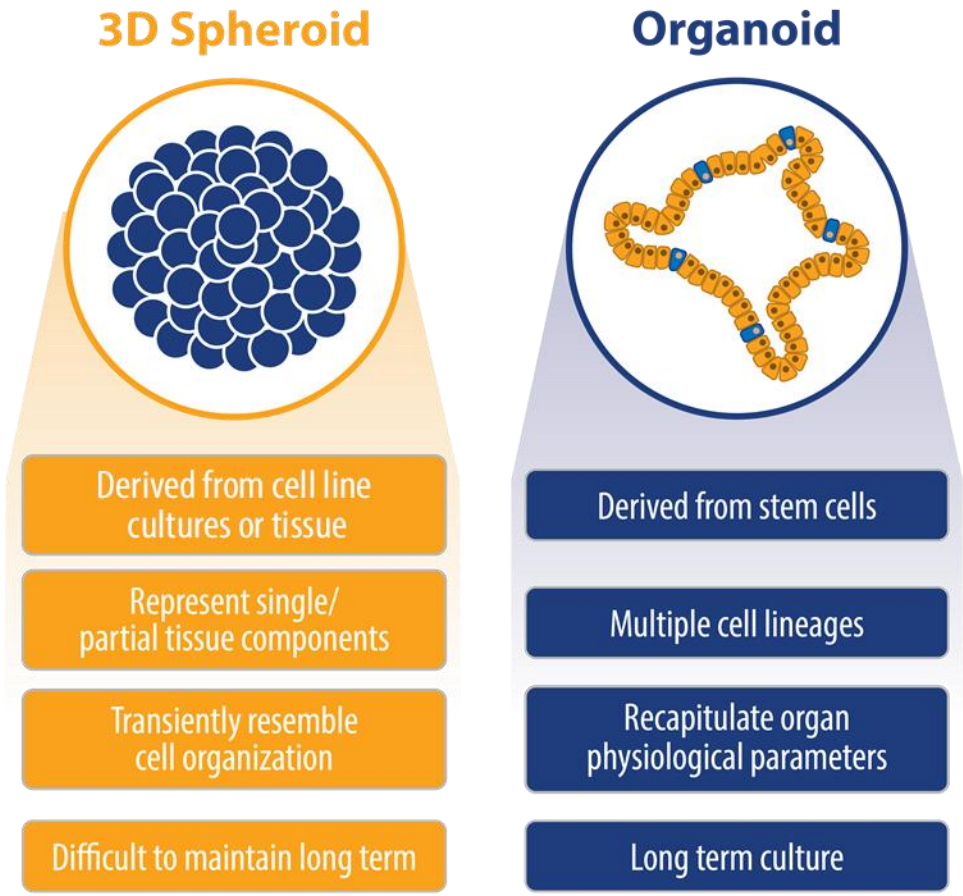
Applications

- Investigate target engagement, oncogenic pathways, MoA
- HTS – lead identification
- Workhorse models for lead optimization
- Non-translational studies

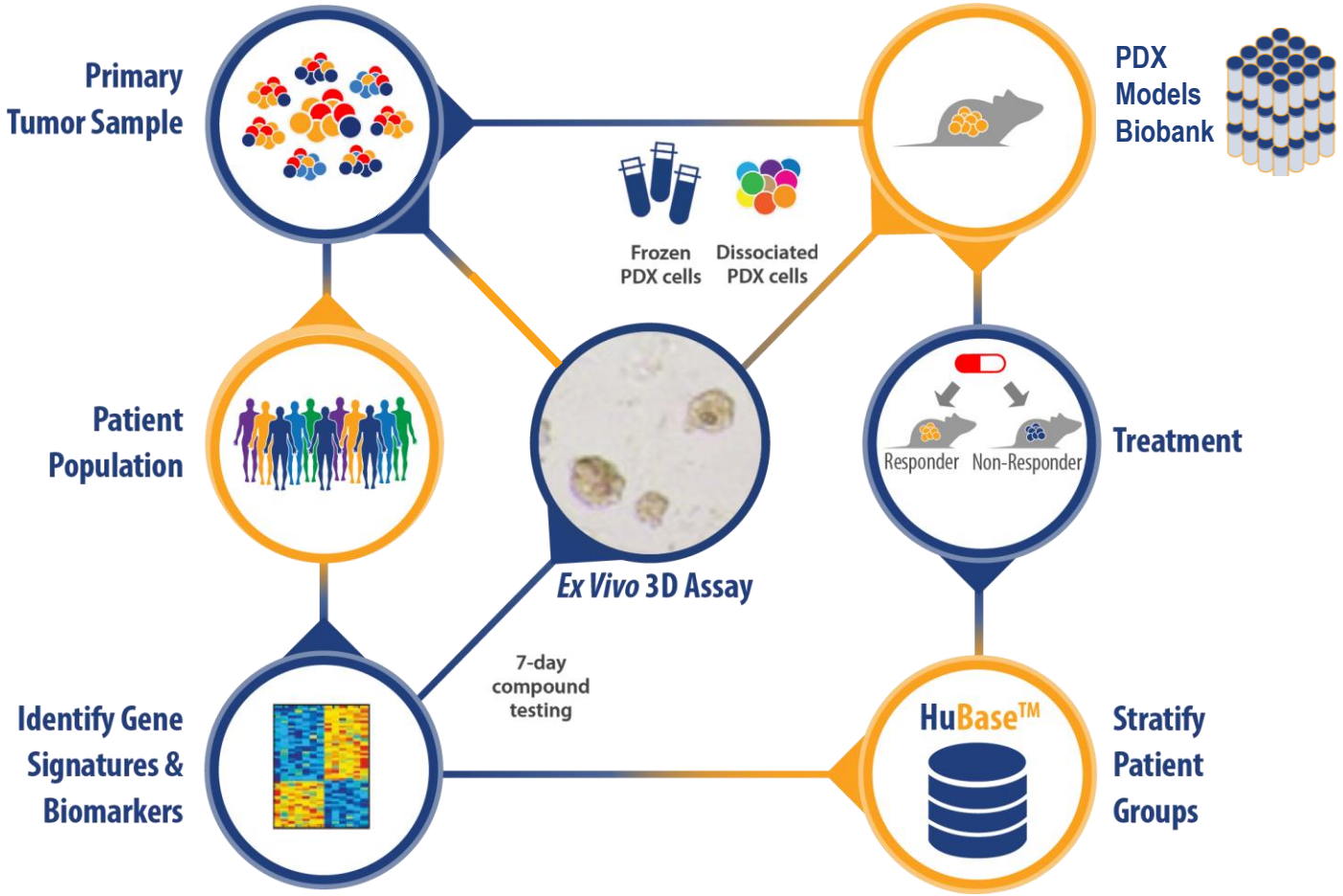
When to Choose Organoids

SELECTING A RELEVANT 3D SYSTEM

Difference Between Spheroids and Organoids



3D Screen Using *Ex Vivo* PDX

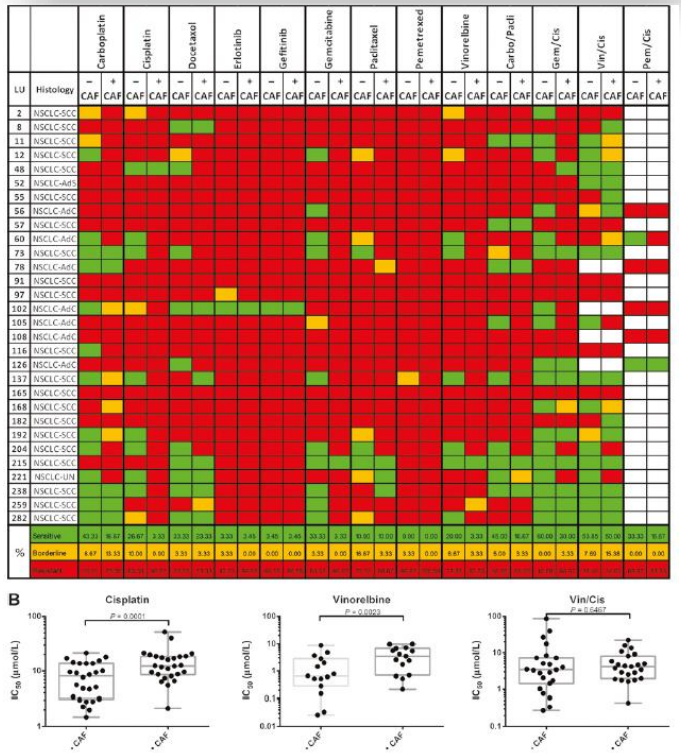



Models and Technologies

Molecular Cancer Therapeutics

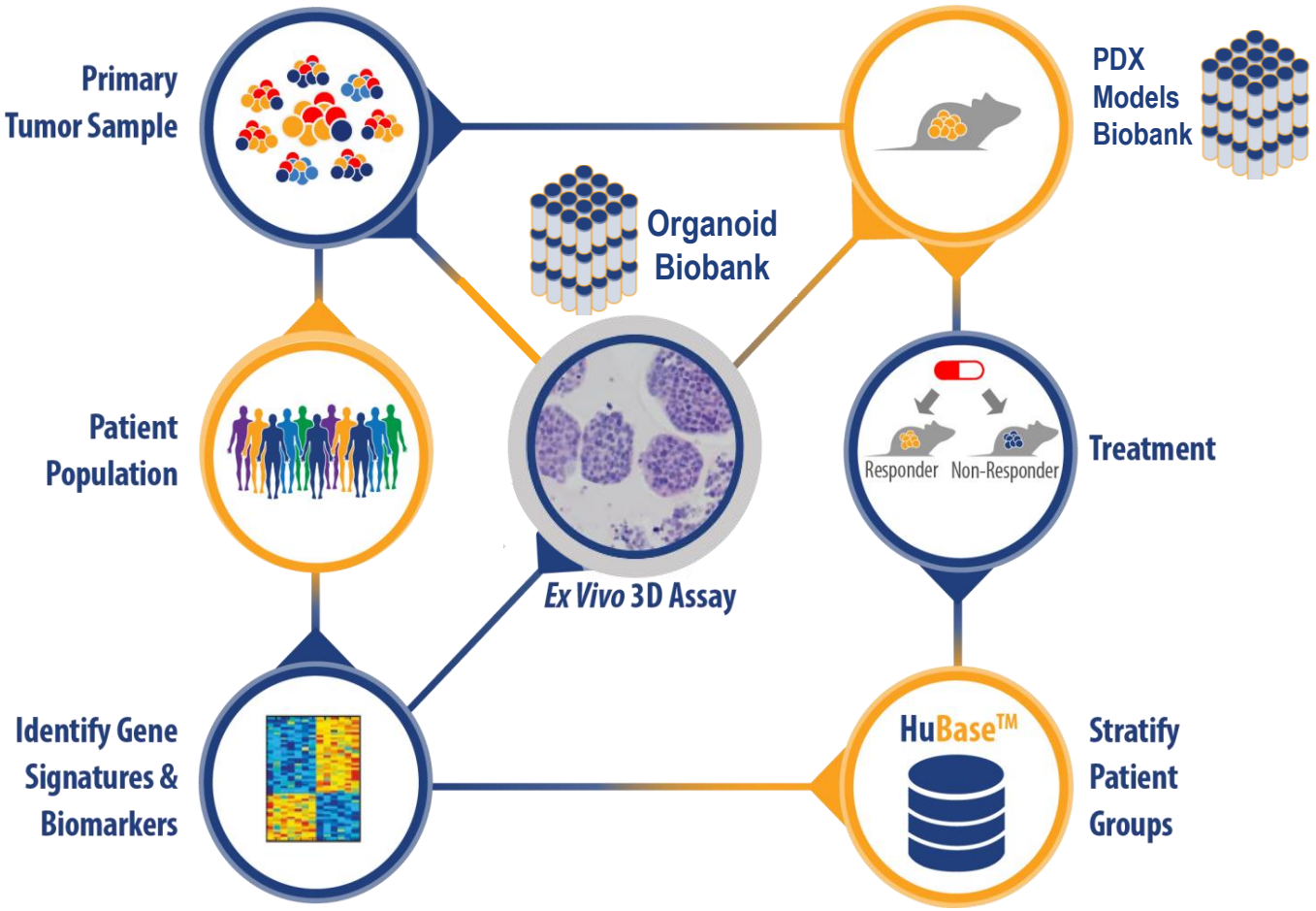
3-Dimensional Patient-Derived Lung Cancer Assays Reveal Resistance to Standards-of-Care Promoted by Stromal Cells but Sensitivity to Histone Deacetylase Inhibitors

David Onion[1,2], Richard H. Argent[1], Alexander M. Reece-Smith[1], Madeleine L. Craze[1], Robert G. Pineda[1], Philip A. Clarke[1], Hari L. Ratan[3], Simon L. Parsons[4], Dileep N. Lobo[5], John P. Duffy[6], John C. Atherton[3], Andrew J. McKenzie[7], Rajendra Kumari[7], Peter King[8], Brett M. Hall[8], and Anna M. Grabowska[1]



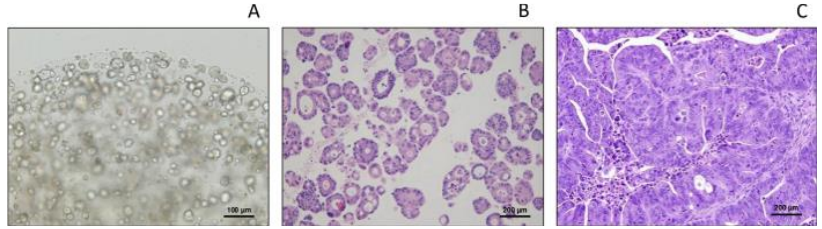
Onion *et al* 2016 Mol Can Therapeutics

3D Screen Using *In Vitro* Organoids

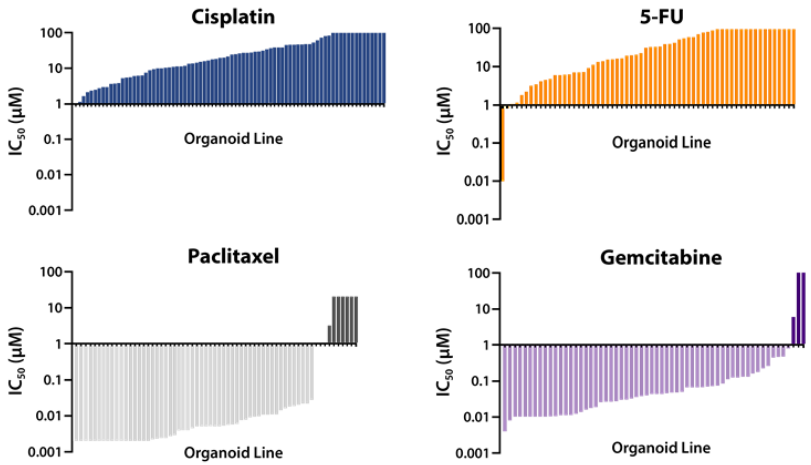


Creating Matched In vivo/In vitro Patient-Derived Model Pairs of PDX and PDX-Derived Organoids for Cancer Pharmacology Research

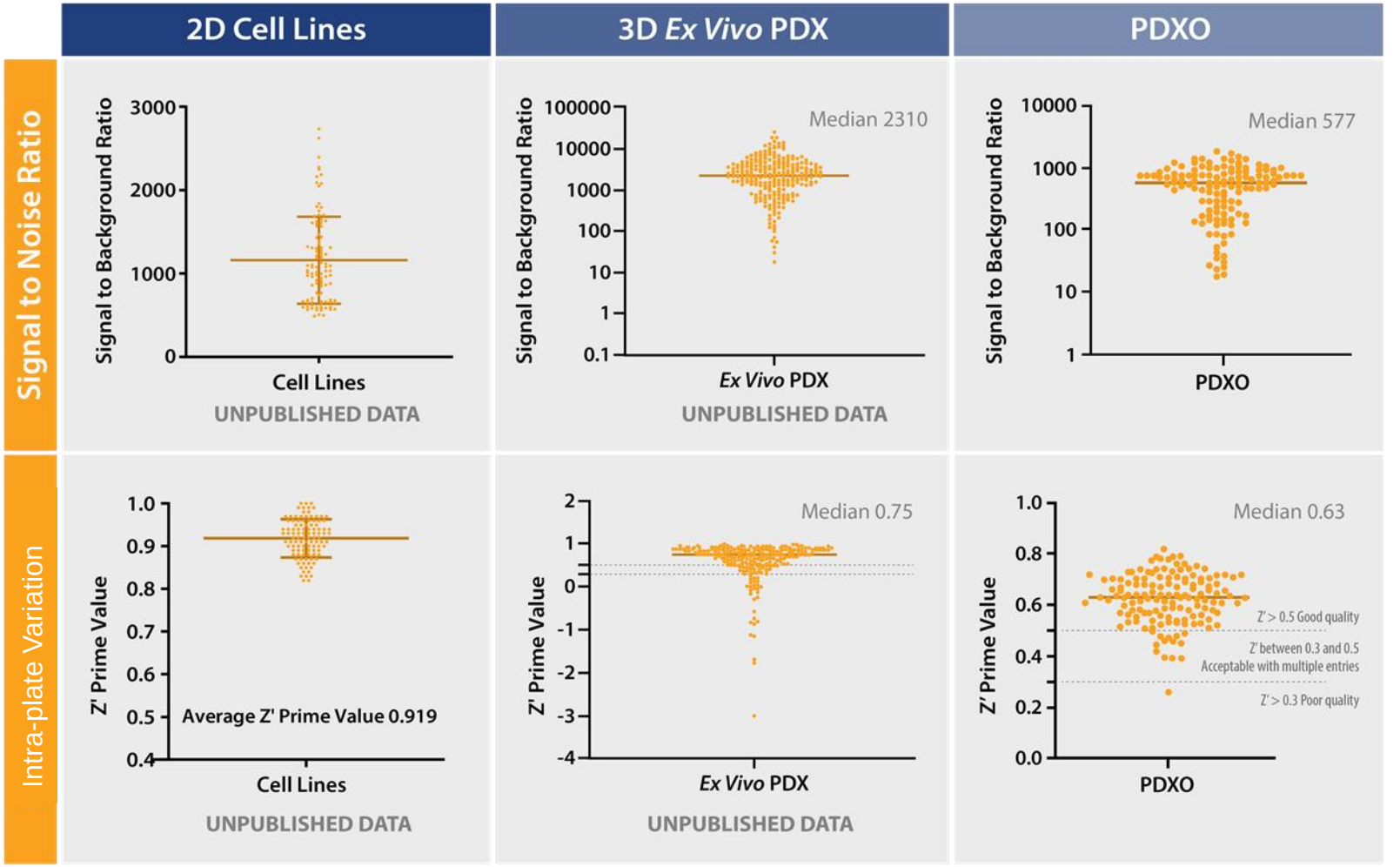
Xiaoxi Xu[1], Limei Shang[1], Shuzong Wang[2], Jun Zhou[2], Xuesong Ouyang[2], Meiling Zheng[1], Binchen Mao[2], Likun Zhang[2], Xiaobo Chen[1], Jingjing Wang[2], Jing Chen[3], Wubin Qian[2], Sheng Guo[2], Yujun Huang[2], Qi-Xiang Li[3]



Xu *et al* 2020 JOVE in press



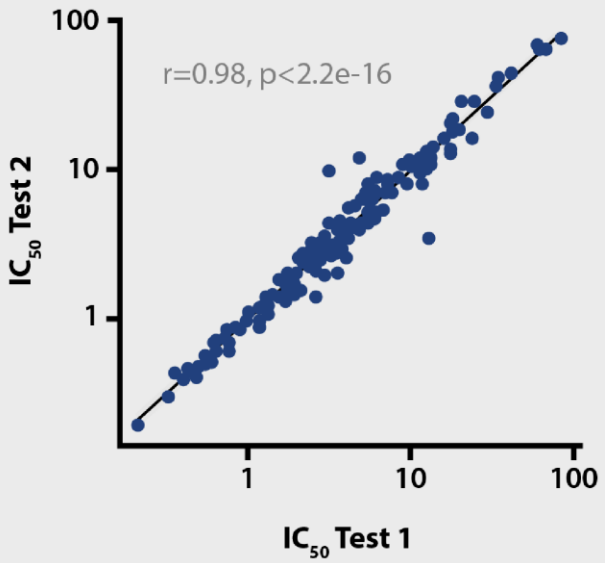
Assay Validation Comparison



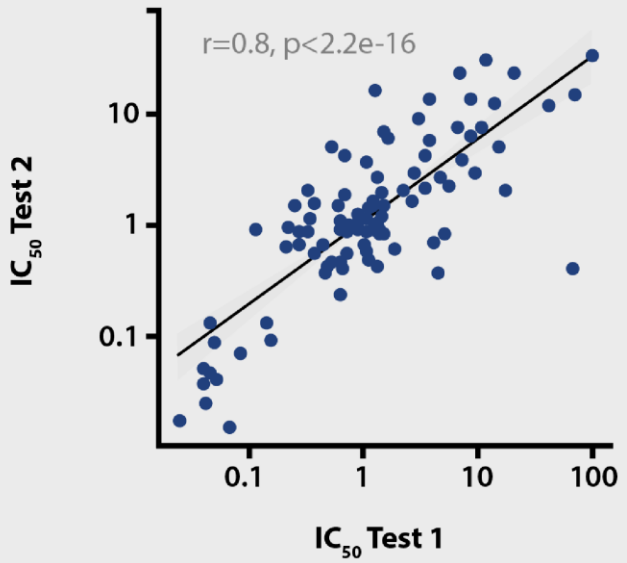
Inter-plate Variation Comparison

Inter-plate Variation (IC_{50})

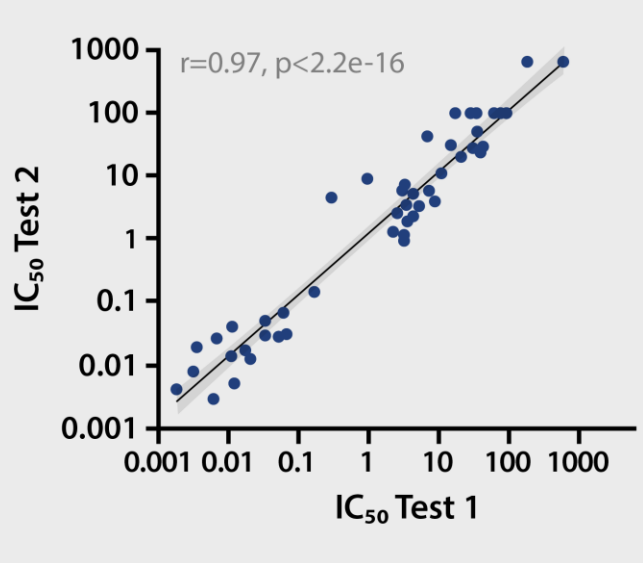
2D Cell Lines



3D *Ex Vivo* PDX



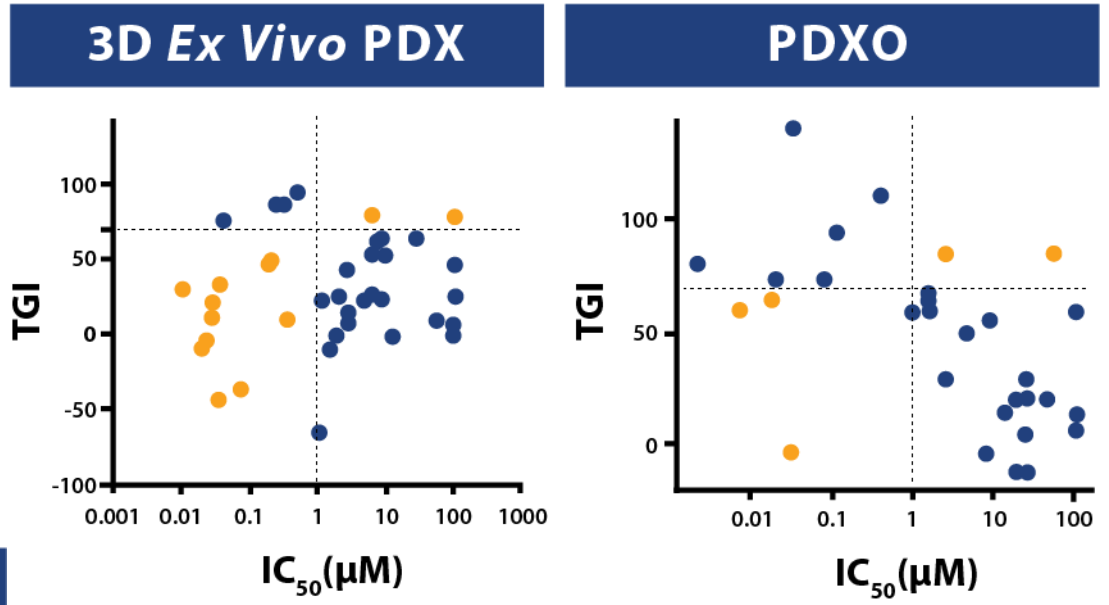
PDXO



UNPUBLISHED DATA

Correlation with *In Vivo* Response

- PDXO have a higher prediction power of corresponding *in vivo* PDX response compared to 3D *ex vivo* PDX assay



Overall prediction 68%
Fisher's exact test p value = 0.17

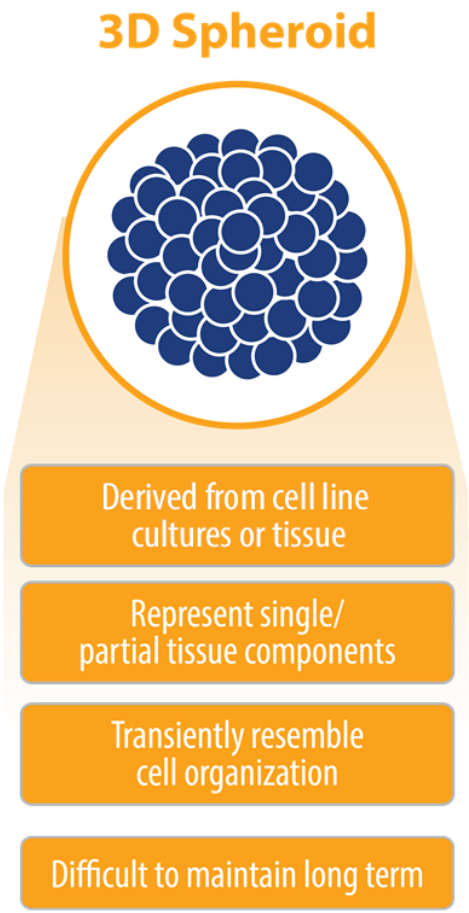
TGI \ IC_{50}	Sensitive (IC_{50}<1μM)	Resisant (IC_{50}≥1μM)
Sensitive (TGI≥70%)	4 (Positive prediction 27%)	2
Resistant (TGI<70%)	11	23 (Negative prediction 92%)

Overall prediction 86%
Fisher's exact test p value = 0.001135

TGI \ IC_{50}	Sensitive (IC_{50}≥1μM)	Resisant (IC_{50}≥1μM)
Sensitive (TGI≥70%)	6 (Positive prediction 75%)	2
Resistant (TGI<70%)	2	20 (Negative prediction 91%)

UNPUBLISHED DATA

Why Use 3D Cell-Based Models?



Advantages

- Suitable for wide range of cells/tissue & co-culture conditions
- More closely mimic tissue architecture
- Greater physiological relevance
- Enhanced translatability, compared to 2D models

Limitations

- Unstable in long-term culture, due to cellular senescence
- Lower reproducibility and translatability *in vivo*
- Limited tissue availability can challenge scalability
- Automation achievable but lower throughput than 2D

Applications

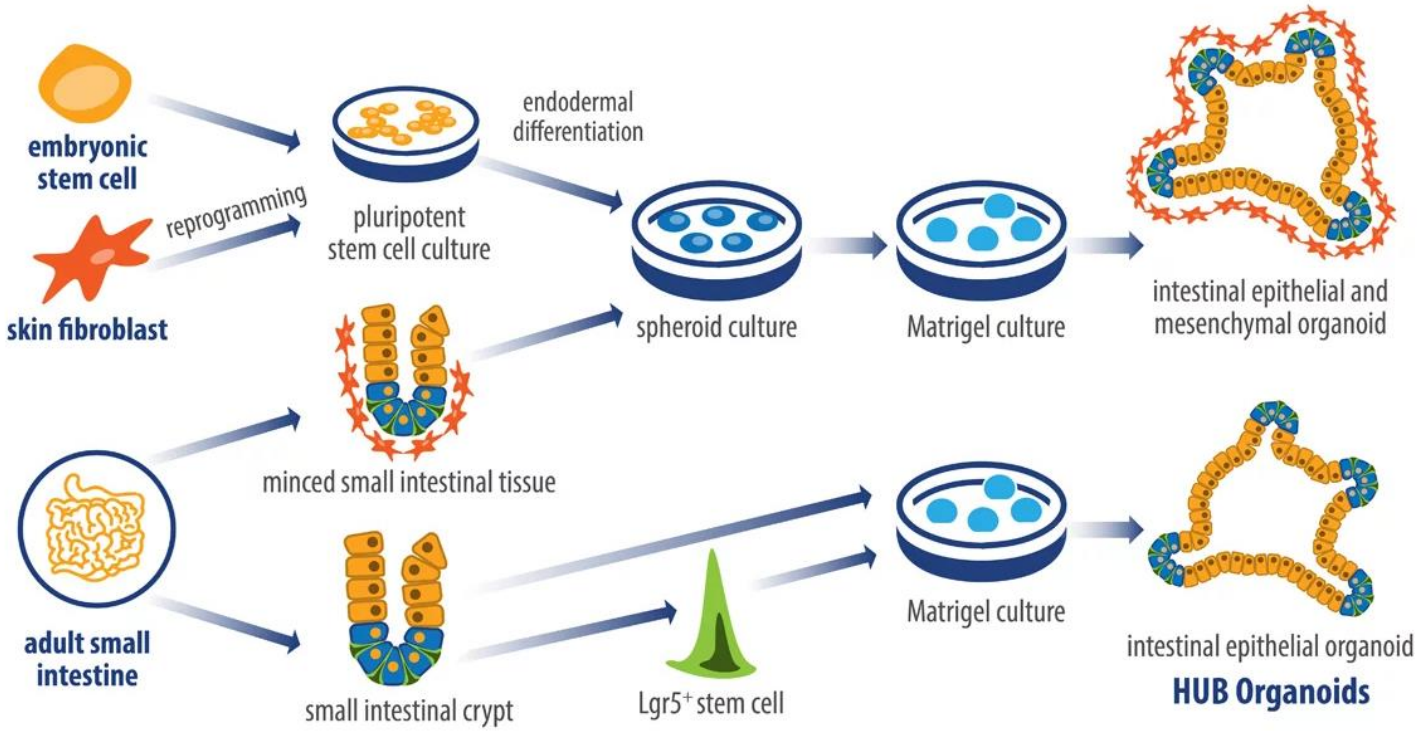
- Investigate efficacy, target engagement, oncogenic pathways, MoA in relevant TME
- CSCs, hypoxia and drug penetrance
- Clinical hypotheses testing and screening in primary tissue

Quick Tips

WHICH ORGANOID SYSTEM?

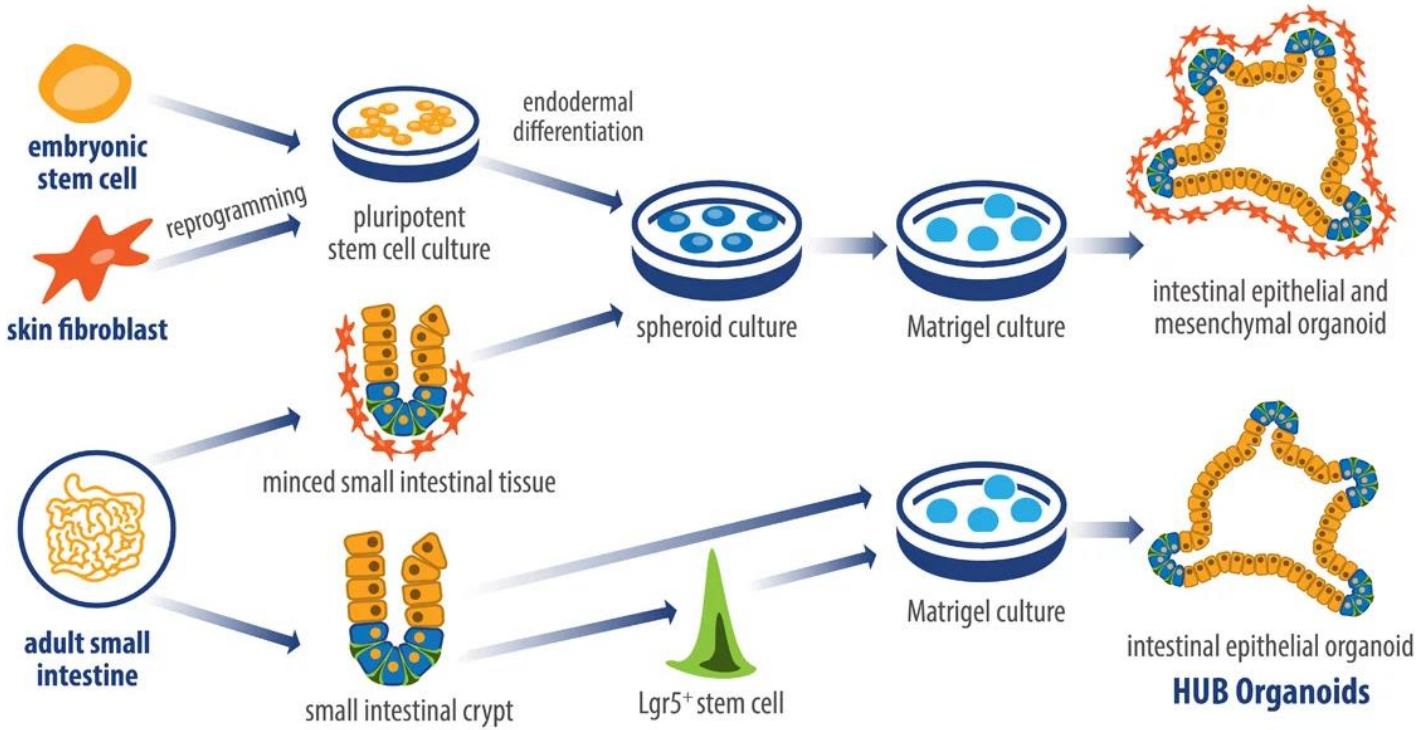
The advantage of HUB Organoid Technology

- Pure epithelial compartment; absence of mesenchymal cellular niche
- More robust and genomically stable; faster establishment
- The only **cancer patient-relevant** technology

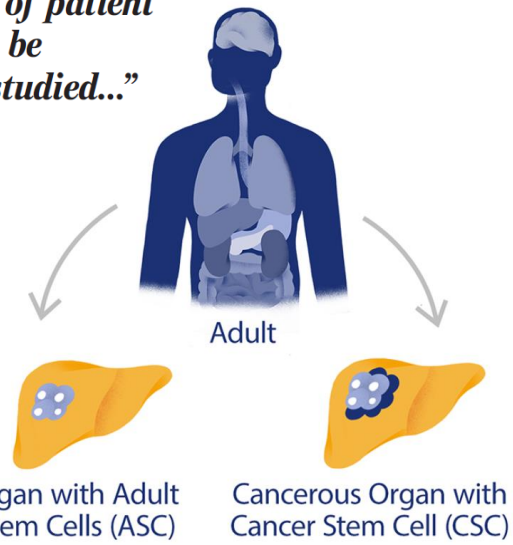


The advantage of HUB Organoid Technology

- Pure epithelial compartment; absence of mesenchymal cellular niche
- More robust and genomically stable; faster establishment
- The only **cancer patient-relevant** technology



"...PDO biobanks greatly expand the types of patient samples that can be propagated and studied..."



Organoids Predict Clinical Response

- Translatable models with demonstrated predictive power of clinical response

Vlachogiannis *et al.*, *Science* **359**, 920–926 (2018)

RESEARCH | REPORTS

ORGANOIDS

Patient-derived organoids model treatment response of metastatic gastrointestinal cancers

Georgios Vlachogiannis,[1] Somaieh Hedayat,[1] Alexandra Vatsiou,[2] Yann Jamin,[3] Javier Fernández-Mateos,[1,2] Khurum Khan,[1,4] Andrea Lampis,[1] Katherine Eason,[1] Ian Huntingford,[1] Rosemary Burke,[5] Mihaela Rata,[3] Dow-Mu Koh,[3,6] Nina Tunariu,[3,6] David Collins,[3] Sanna Hulkki-Wilson,[1] Cha… Sing Yu Moorcraft,[4] Ian Chau,[4] Sheela Rao… Maria Bali,[3,6] Mahnaz Darvish-Damavandi… Elizabeth C. Smyth,[4] Ruwaida Begum,[4] Pau… Mitchell Dowsett,[7] Johann de Bono,[8] Paul … Matteo Fassan,[9] Owen J. Sansom,[10] Suzanne Eccles,[5] Naureen Starling,[4] Chiara Braconi,[4,5] Andrea Sottoriva,[2] Simon P. Robinson,[3] David Cunnin…

- 90% positive prediction
- 100% negative prediction

Ooft *et al.*, *Sci. Transl. Med.* **11**, eaay2574 (2019)

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Patient-derived organoids can predict response to chemotherapy in metastatic colorectal cancer patients

Salo N. Ooft[1,2]*, Fleur Weeber[1,2]*, Krijn K. Dijkstra[1,2†], Chelsea M. McLean[1,2†], Sovann Kaing[1,2], Erik van Werkhoven[3], Luuk Schipper[1,2], Louisa Hoes[1,2], Daniel J. Vis[2,4], Joris van de Haar[1,2,4], Warner Prevoo[5], Petur Snaebjornsson[6], Daphne van der Velden[1,2‡], Michelle Klein[1,2], Myriam Chalabi[1], Henk Boot[7], Monique van Leerdam[7], Haiko J. Bloemendal[8], Laurens V. Beerepoot[9], Lodewyk Wessels[2,4,10], Edwin Cuppen[2,11,12], Hans Clevers[2,13,14], Emile E. Voest[1,2,7§]

TheScientist

EXPLORING LIFE, INSPIRING INNOVATION

NEWS & OPINION MAGAZINE

Home / News & Opinion

Tumor Organoids Predict How Well Patients Respond to Cancer Drugs

Testing treatments on mini tumors may save time in identifying which therapies work best, a new study s…

Feb 22, 2018
RUTH WILLIAMS

In 100 percent of cases, if a drug didn't work on a patient's organoids, then it didn't work in the patient, and in nearly 90 percent of cases, if a drug did work on the organoids, then it worked in the patient.

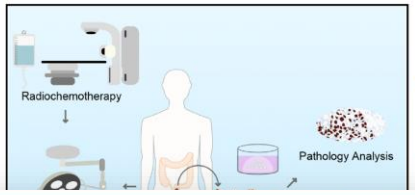
Yao et al., 2020, Cell Stem Cell *26*, 1–10

Clinical and Translational Report

Cell Stem Cell

Patient-Derived Organoids Predict Chemoradiation Responses of Locally Advanced Rectal Cancer

Graphical Abstract



Authors

Ye Yao, Xiaoya Xu, Lifeng Yang, ..., Hans Clevers, Zhen Zhang, Guoqiang Hua

Correspondence

zhenzhang6@gmail.com (Z.Z.), guoqianghua@fudan.edu.cn (G.H.)

In Brief

Yao et al. generated a patient-derived …iobank from patients …ced rectal cancer …ted that organoids had … profiles to those of the … that PDOs can predict …moradiation responses, …alue as a companion … LARC treatment.

nature medicine

RESOURCE

https://doi.org/10.1038/s41591-019-0584-2

Ganesh *et al.*, 2019 Nature Medicine

A rectal cancer organoid platform to study individual responses to chemoradiation

Karuna Ganesh[1,2,21], Chao Wu[3,4,21], Kevin P. O'Rourke[5,6], Bryan C. Szeglin[4,7], Youyun Zheng[8,9], Charles-Etienne Gabriel Sauvé[4], Mohammad Adileh[4], Isaac Wasserman[4], Michael R. Marco[4], Amanda S. Kim[10], Maha Shady[8,9], Francisco Sanchez-Vega[4,11], Wouter R. Karthaus[3], Helen H. Won[8,9], Seo-Hyun Choi[4], Raphael Pelossof[4], Afsar Barlas[12], Peter Ntiamoah[8], Emmanouil Pappou[4], Arthur Elghouayel[4], James S. Strong[4], Chin-Tung Chen[4], Jennifer W. Harris[4], Martin R. Weiser[4], Garrett M. Nash[4], Jose G. Guillem[4], Iris H. Wei[4], Richard N. Kolesnick[1], Harini Veeraraghavan[13], Eduardo J. Ortiz[14], Iva Petkovska[14], Andrea Cercek[2], Katia O. Manova-Todorova[12], Leonard B. Saltz[2], Jessica A. Lavery[15], Ronald P. DeMatteo[16], Joan Massagué[5], Philip B. Paty[4], Rona Yaeger[2], Xi Chen[17], Sujata Patil[15], Hans Clevers[18], Michael F. Berger[8,9], Scott W. Lowe[5], Jinru Shia[8,19], Paul B. Romesser[10], Lukas E. Dow[20], Julio Garcia-Aguilar[4], Charles L. Sawyers[3,21*] and J. Joshua Smith[3,4,21*]

CrownBio Organoid Biobank

The only available organoid biobank for preclinical oncology developed using HUB's well-established, patented organoid technology

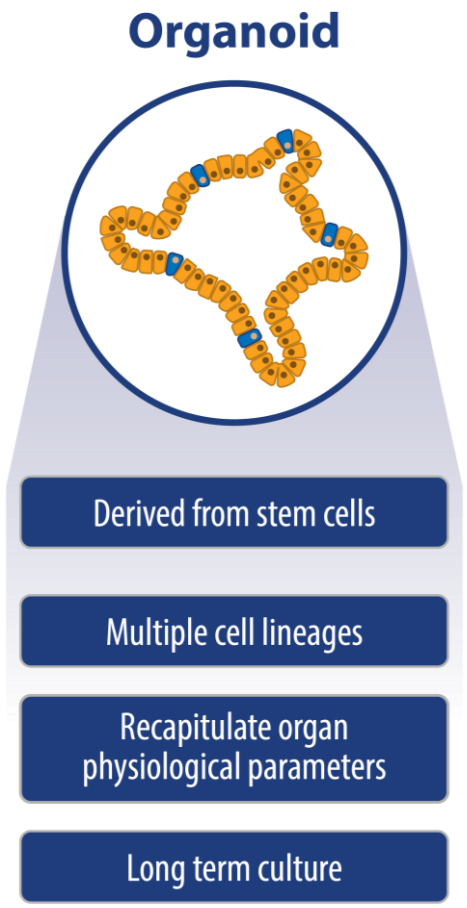
PDX-derived organoids (PDXO)

- Built using CrownBio PDX collection as a source of human tissue to complement HUB organoid collection
- **>180 models** in our master biobank over **15 cancer types**
- Matched *in vivo* PDX models
- HTS screening platform available
- Panels of models with oncogenic driver mutations

HUB patient-derived organoids (PDO)

- Models transferred from HUB include breast, colorectal, lung, and pancreatic cancer organoids
- Rapidly expanding collection of **>180 models**
- Key collection features include:
  - Primary and metastatic matched pairs
  - Normal and tumor matched pairs
  - Models capturing heterogeneity of the patient tumor
  - Panels of models with oncogenic driver mutations

Why use Use Tumor Organoids?



Advantages

- Clinically predictive models
- Greater physiological relevance
- Scalable, amenable to biobanking & engineering
- Highly reproducible with automation achievable for HTS
- Normal and disease tissue organoids

Limitations

- More complex to establish than 2D
- Automation has lower throughput than 2D
- Epithelial origins or model not yet available

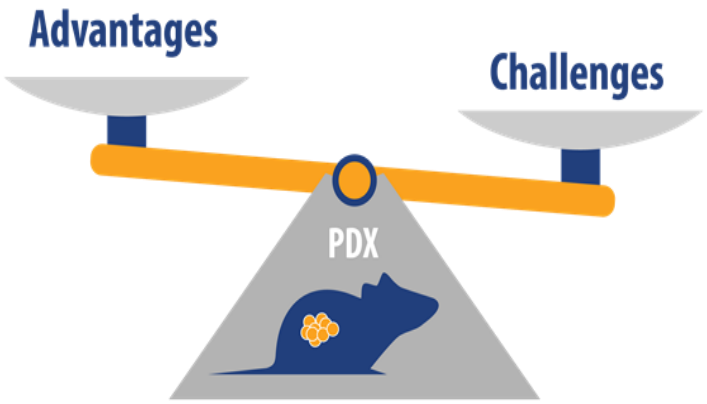
Applications

- Matrix HTS or clinical trial in a dish
- Matched or labelled *in vivo* models
- Target validation, engineer TAA, biomarker identification
- Potential for matched normal tissue for on/off target effects
- Co-culture with immune cells or stromal cells for relevant TME

Advantages & Limitations

DO 3D SYSTEMS REPLACE IN VIVO MODELS?

Why Use *In Vivo* PDX Models?



Advantages

- Clinically predictive models
- Greater physiological relevance and patient diversity
- Large biobanks enable mouse clinical trials to be conducted

Limitations

- Ethical – clinical & animal welfare
- Longer to establish than organoids & lower throughput than 3D
- Favourable for more aggressive tumors
- Limited matched *in vitro* models
- Limited applicability to immuno-oncology

Applications

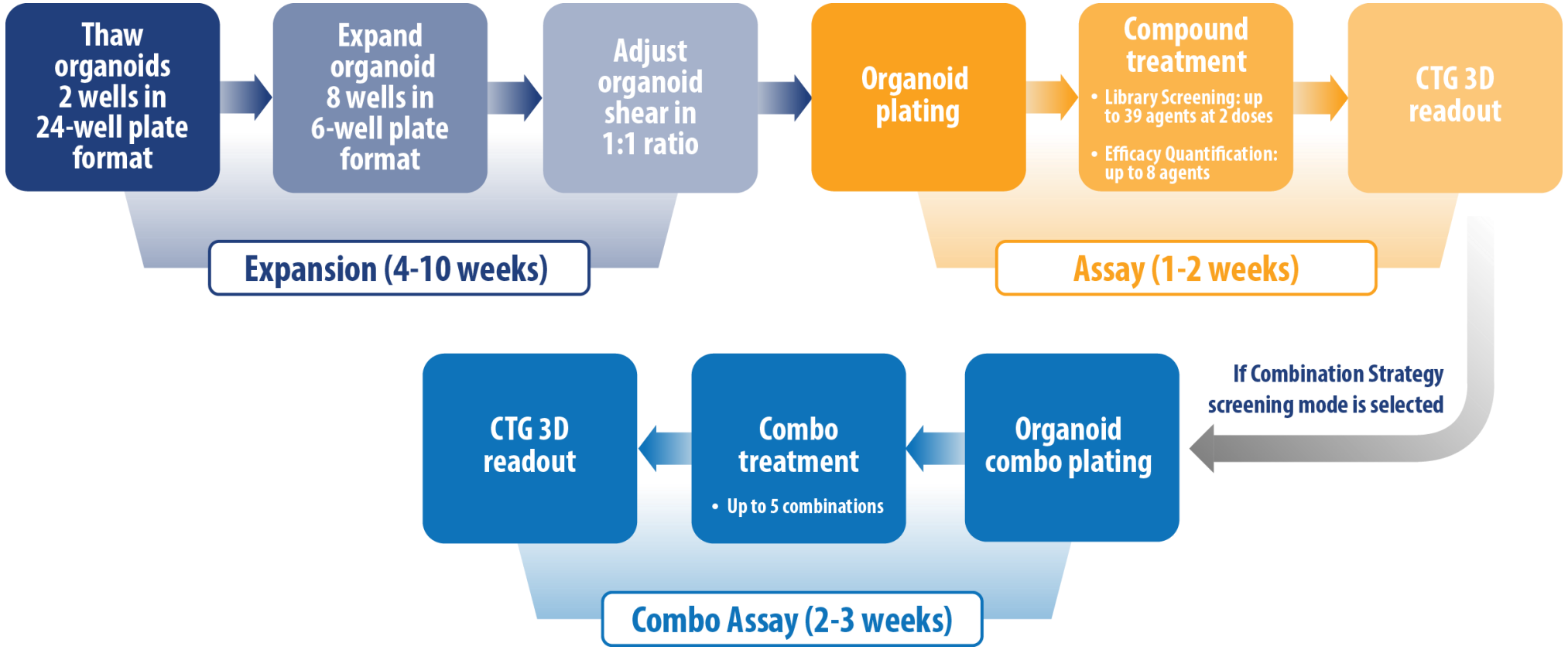
- Mouse clinical trial
- Efficacy or combination evaluation
- PK/PD
- Evaluate SoC, targeted agents, cellular therapies and more
- Humanized models to evaluate immune modulators

Feasibility Study

EVALUATE SYNERGISTIC EFFECTS USING A PDXO SCREENING PLATFORM

Organoid Screen Workflow

- Screen multiple compounds using either a single concentration, multiple concentrations or combinations across multiple patients



Study Objective

- Evaluate the feasibility of a **PDXO-based screening platform** to test potential synergistic effects of 2 compounds
- Validate **matrix screen** set up
  - Multiple combination strategies, dosing and models tested in parallel
- Analyze the data using **two independent mathematical models** for additional confidence

Background and Significance

- Synergies between the WEE1 inhibitor MK-1775 and the CHK inhibitor MK-8776, and each with gemcitabine, have been reported for the treatment of ***p53* mutant pancreatic cancer** as well as other cancer types

Mechanistic Distinctions between CHK1 and WEE1 Inhibition Guide the Scheduling of Triple Therapy with Gemcitabine

Siang-Boon Koh, Yann Wallez, Charles R. Dunlop, Sandra Bernaldo de Quirós Fernández, Tashinga E. Bapiro, Frances

DOI: 10.1158/0008-5472.CAN-17-3932 Published June 2018 Check for updates

MK-1775, a Potent Wee1 Inhibitor, Synergizes with Gemcitabine to Achieve Tumor Regressions, Selectively in p53-Deficient Pancreatic Cancer Xenografts

N.V. Rajeshkumar, Elizabeth De Oliveira, Niki Ottenhof, James Watters, David Brooks, Tim Demuth, Stuart D. Shumway, Shinji Mizuarai, Hiroshi Hirai, Anirban Maitra, and Manuel Hidalgo

DOI: 10.1158/1078-0432.CCR-10-2580 Published May 2011

Dose Escalation Trial of the Wee1 Inhibitor Adavosertib (AZD1775) in Combination With Gemcitabine and Radiation for Patients With Locally Advanced Pancreatic Cancer

Kyle C. Cuneo, MD[1]; Meredith A. Morgan, PhD[1]; Vaibhav Sahai, MBBS, MS[1]; Matthew J. Schipper, PhD[1]; Leslie A. Parsels, PhD[1]; Joshua D. Parsels[1]; ...

Unique functions of CHK1 and WEE1 underlie synergistic anti-tumor activity upon pharmacologic inhibition

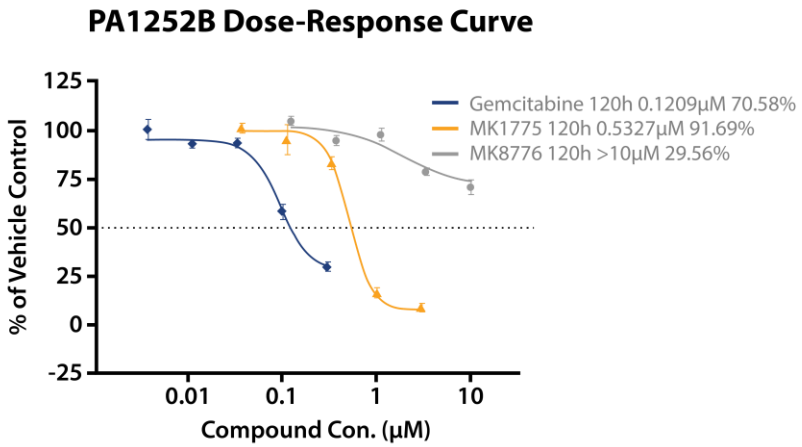
Amy D Guertin, Melissa M Martin, Brian Roberts, Melissa Hurd, Xianlu Qu, Nathan R Miselis, Yaping Liu, Jing Li, Igor Feldman, Yair Benita, Andrew Bloecher, Carlo Toniatti & Stuart D Shumway

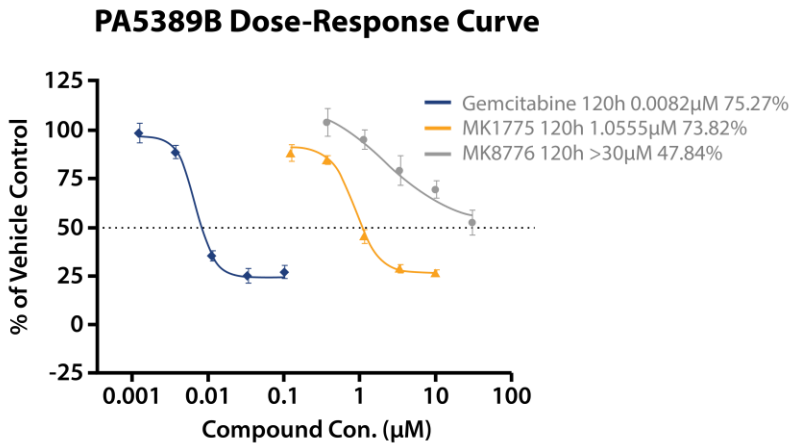
Cancer Cell International **12**, Article number: 45 (2012) | Cite this article

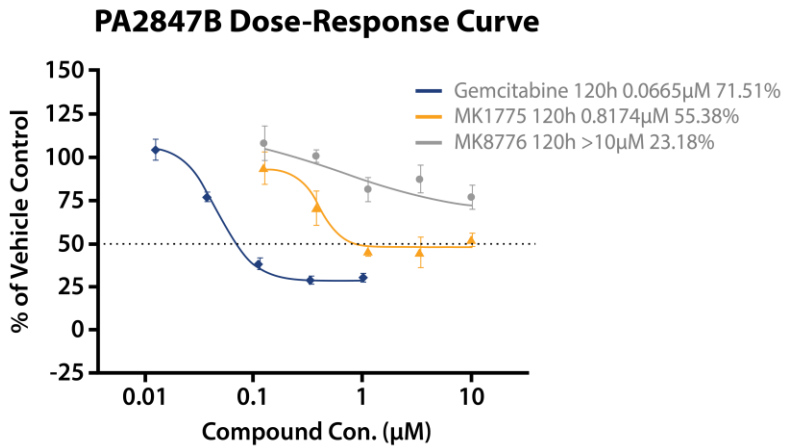
8270 Accesses | **51** Citations | **1** Altmetric | Metrics

Model Selection

- *p53* mutant PDXO models selected similar models to published studies
  - PA5389B and PA1252B with a $p53^{R282W}$ and $p53^{R273H}$ missense mutation, respectively
  - PA2847B with a $p53^{W91Ter}$ nonsense mutation
- Dose response curves initially established for single agents
- All models were:
  - Sensitive to gemcitabine [IC_{50}<0.2μM] and MK-1775 [IC_{50}<1μM]
  - Poor sensitivity to MK-8776 [IC_{50}>10μM]





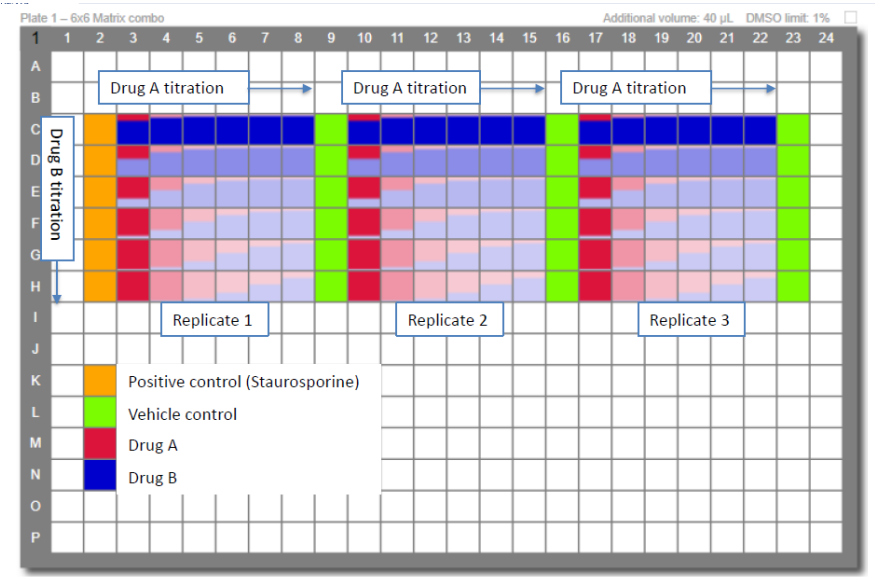


Combination Study Design

- 3 combination strategies
- 6-point titration of each inhibitor combined in a 6×6 matrix format, for 5 days
- 3 different PDXO models
- Cell viability measured
- 2 independent mathematical models of synergy (Bliss and Loewe) used to assess the combination effect
  - Synergy score >5 indicates synergistic effect
  - Synergy score <5 indicates antagonism

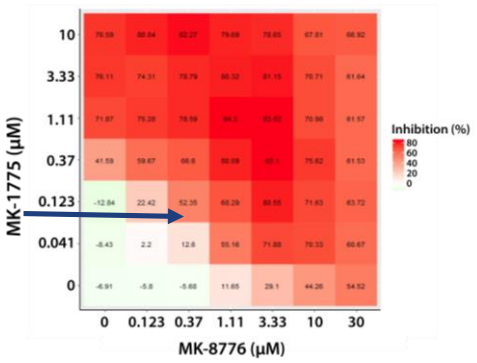
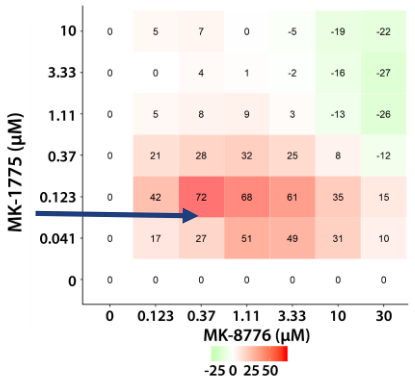
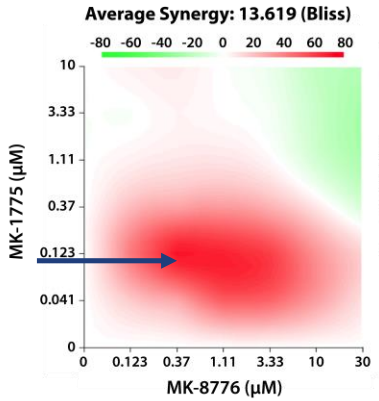
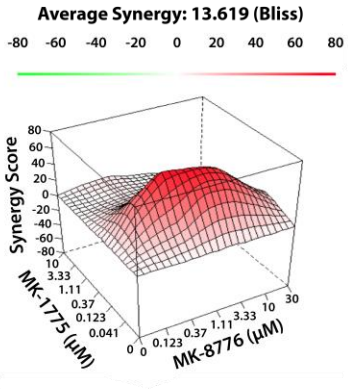
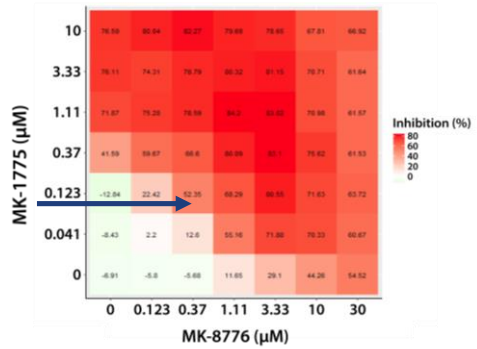
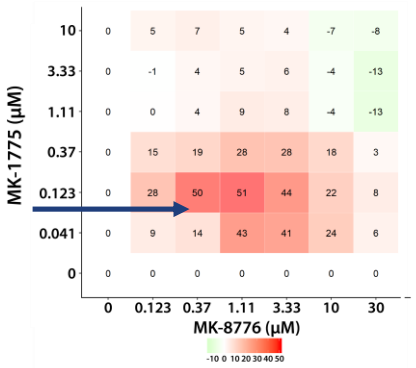
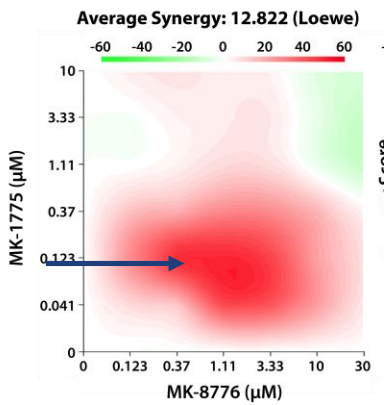
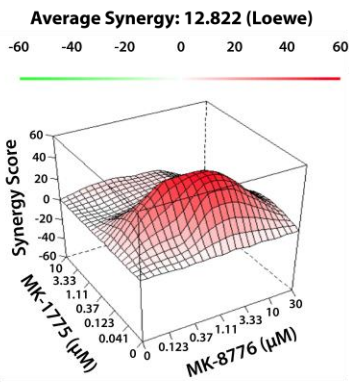
	Drug 1	Drug 2
Combo 1	MK-1775	MK-8776
Combo 2	Gemcitabine	MK-8776
Combo 3	Gemcitabine	MK-1775

6×6 matrix, 1 model/plate
MK-1775: max [Conc] = 10μM; dilution factor 3
MK-8776: max [Conc] = 30μM; dilution factor 3



Example of Matrix Design Results

- Combination of MK-1775+MK-8776 analyzed by both Bliss and Loewe methods showed strong synergy at low concentrations (PA5389B pancreatic cancer organoid)

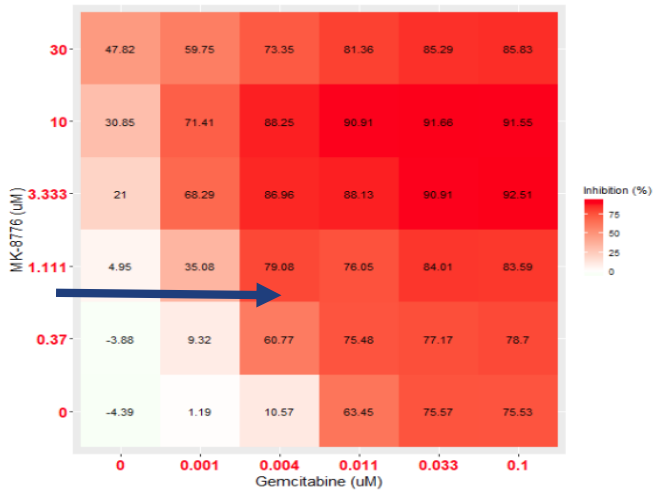
	Dose inhibition heat map	Synergy score heat map	2D contour map	3D response surface plot
Bliss				
Loewe				

Combination with Gemcitabine

- In combination with SoC gemcitabine, the highest synergy scores (>30) were seen with MK-8776/gemcitabine combo, with both mathematical models
- However, some low average values were also observed, suggesting antagonism with certain dose combinations
- MK-8776 achieved a 67-88% growth inhibition at the non-inhibitory concentration of 1.111µM, when in combination with 11-33nM gemcitabine

Model	MK-1775/Gemcitabine				MK-8776/Gemcitabine			
	Highest Synergy Score		Average Synergy Score		Highest Synergy Score		Average Synergy Score	
	Bliss	Loewe	Bliss	Loewe	Bliss	Loewe	Bliss	Loewe
PA5389B	48.8	44.57	8.40	14.95	64.08	56.78	19.92	21.49
PA2847B	32.19	15.34	-4	-5.04	60.1	42.64	11.55	-4.80
PA1252B	58.72	44.75	14.23	12.06	79.31	32.27	70.89	27.61

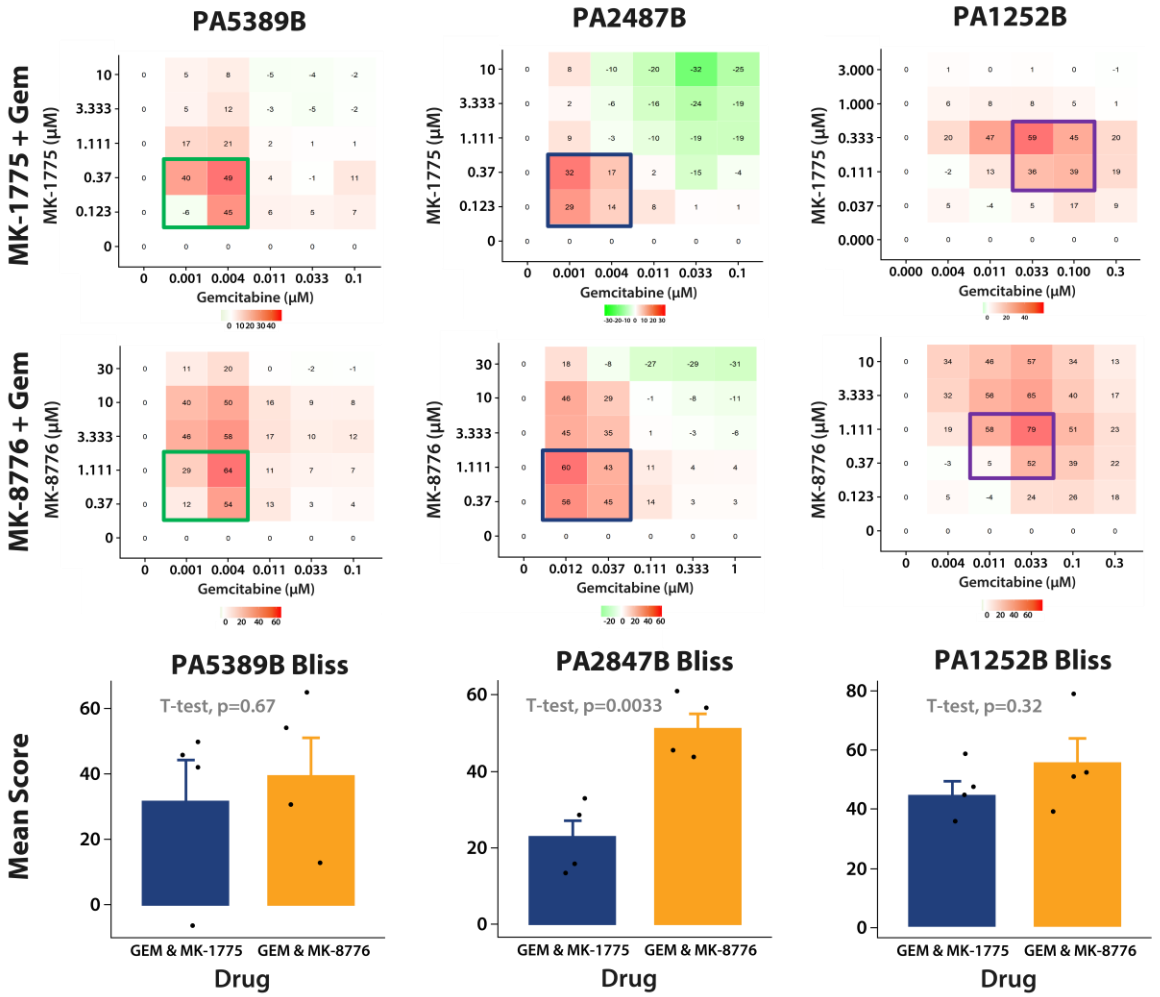
PA5389B dose inhibition heat map



Synergy score >5 indicates synergist effects
Synergy score <5 indicates antagonistic effects

Comparison of Synergy

- Quadrant with highest synergy scores was found to be at lower drug concentrations for the models with p53 missense mutation (PA5389B and PA2487B), compared to PA1252B
- Overall a higher synergy score was observed in the p53 mutated models at lower concentrations
- Bliss analysis also showed MK-1775 + gemcitabine to have a significantly higher mean synergy score than MK-8776 in PA2487 organoid model

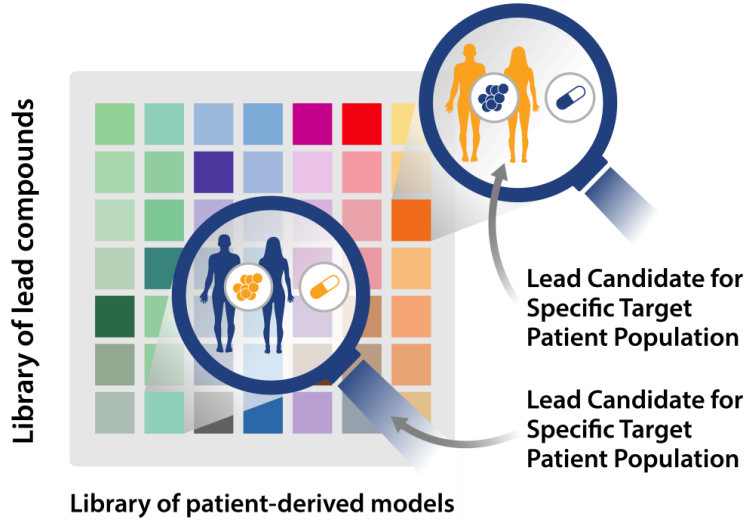


Study Conclusions

- Synergistic effects of MK-1775 (WEE1 inhibitor) and MK-8776 (CHK inhibitor) were assessed in highly patient-relevant p53 mutant pancreatic cancer PDXO models
- Results indicated:
  - All pancreatic cancer PDXO models were sensitive to gemcitabine and MK-1775, and poorly sensitive to MK-8776
  - The combination of MK-1775 and MK-8776 shows very strong synergistic effect in all models tested
  - The synergy observed between MK-8776/gemcitabine was significantly greater than MK-1775/gemcitabine in one of the p53 mutated models (PA2847) at low doses, however antagonism was observed at higher concentrations
- The rapid screening of patient-relevant organoids in a combination matrix approach enables synergistic profiling to be easily conducted, providing valuable insight into combination strategies

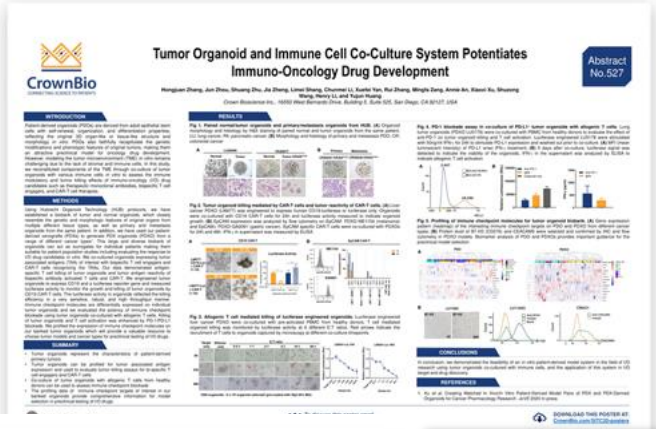
Summary

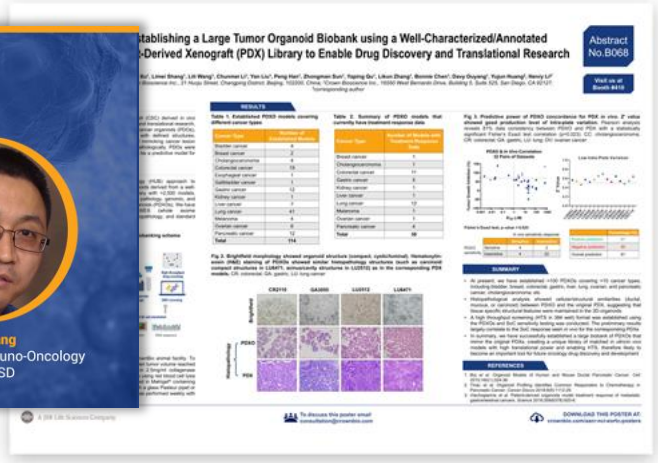
- Patient-relevant models can bridge the gap between the lab and the clinic
- Adoption during early *in vitro* stages can be achieved with 3D models
- However, some 3D tumor spheroid models can lack reproducibility, efficiency and translatability
- In comparison, 3D organoids are “mini-organs in a dish” derived from tissue stem cells, that are highly predictive of the *in vivo* and clinical response
- Adoption of organoids could potentially improve the drug discovery workflow, requiring expansion of biobanks and matched models
- Predicting *in vivo* responses will refine the application of *in vivo* models

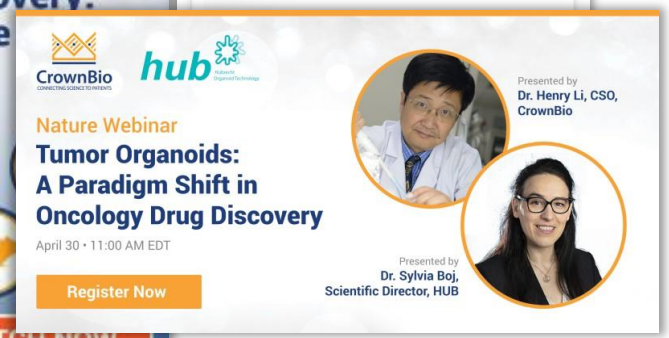


Thank You

- Tumor Organoid Applications to Drug Discovery and Development Resource Library







Clarity With CrownBio

Recognize your next clinical candidate when you see it.

CrownBio
CONNECTING SCIENCE TO PATIENTS