Oncology Cell Panel Screening Platform



WuXi Biology, Oncology & Immunology Unit





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OncoWuXi Newsletter

Highlight

We offer a comprehensive cell screening panel of *over 600 authenticated, well-validated human cancer cell lines across 50 cancer types*. Our cancer cell line panel provides powerful tools for cancer research and drug discovery.

- Flexible and diverse service models: Economic panel package & Customized cell line selection strategy
- High quality cell banking system: mycoplasma-proof, STR verified and RNA-Seq profiled
- Single agent and combination compound screening for potency (% inhibition & EC50) and synergy (combination index CI)
- Professional design with stringent quality control of study results
- A database of cell growth curve and Standard of Care (SoC) validation data provides guidance for cell model selection
- Optional bioinformatics analysis for in-depth mechanism study
- Integrated with downstream pharmacology services, with 340+ CDX models ready-for-use

More than 600 Human Cancer Cell Lines for Panel Screening



Cancer Types by System	Cancer Type	# of cancer type	# of each system	Cancer Types by System	Cancer Typ
Lung	Lung	148	148		Glioblaston
	Colon	36			Neuroblasto
	Liver	19			Medulloblast
	Pancreatic	24		Brain and Nervous System	Astrocytom
	Esophageal	16			Neurofibroma
	Gastric	15			Neuroglion
Digestive	Cecum	6			Neuroepitheli
System	Rectal	4	124		Primitive
	Cholangiocarcin	2	-		neuroectoder
	oma				Melanoma
	Gastrointestinal	1		Chim	Epidermoid Card
	stromal tumor			SKIN	Neuroendocrin
	Duodenal cancer	1			carcinoma
	Lymphoma	52	103	Urinary	Bladder
Blood	Leukemia	40		System	Kidney
and	Myeloma	10		Bone and	Osteosarcor
Lymph	Thymic	1			Rhabdomyosar
System	carcinoma				Ewings Sarco
Breast	Breast	71	71	Tissue	Synovial sarce
	Ovarian	21		Head and	Fibrous Histiocy
	Endometrial	14	55		Fibrosarcon
Reproduc tive System	Cervix	8			Head and No
	Uterus Sarcoma	3			Tongue
	Gestational	1			Mouth
	choriocarcinoma				Nasal septu
	Prostate	7		Neck	Nasopharyngeal
	Testicular germ	1			Pharyngea
	cell tumor	T			Salivary gla

Cancer Types by System	Cancer Type	# of cancer type	# of each system	
	Glioblastoma	9		
	Neuroblastoma	8		
	Medulloblastoma	4		
Brain and	Astrocytoma	3		
Nervous	Neurofibromatosis	2	29	
System	Neuroglioma	1		
	Neuroepithelioma	1		
	Primitive	1		
	neuroectodermal	L		
	Melanoma	24	26	
Skin	Epidermoid Carcinoma	1		
	Neuroendocrine skin	1		
	carcinoma	-		
Urinary	Bladder	15	25	
System	Kidney	10		
	Osteosarcoma	7	-	
Bone and	Rhabdomyosarcoma	6		
Soft	Ewings Sarcoma	3	21	
Tissue	Synovial sarcoma	3		
	Fibrous Histiocytoma	1		
	Fibrosarcoma	1		
Head and Neck	Head and Neck	2		
	Tongue	4		
	Mouth	1		
	Nasal septum	1	12	
	Nasopharyngeal cancer	1		
	Pharyngeal	2		
	Salivary gland	1		
Endocrine	Thyroid	6	7	
System	Adrenal	1		
Eye	Retinoblastoma	2	2	

Cancer Types by System

- 623 human cancer cell lines derived from 12 systems, totally 52 cancer types, 340+ with CDX model, and 406 RNA-Seq profiled
- 400 with 7-day growth curve (IncuCyte/CTG),
 450 have been used for compound profiling
- High quality cell lines banked at early passage (P2-P10), all Mycoplasma negative and identified by Short Tandem Repeat (STR) profiling
 - Well organized by LabVantage Biobanking System

Standard Practice for Panel Profiling





- LabVantage Biobanking System with high quality cell storage source
- Standardized cell recovery and culture to ensure the cells are in good condition and in the logarithmic growth phase
- Appropriate seeding density according to the growth curve and cell doubling time
- Target-based customized protocol and plate map design for dosages and treatment time

- Systematic compound manage and storage model
- Proper vehicle selection based on the nature of test article
- Diversified automatic dosing system for both aqueous or organic solution
- Cross QC for compound position

- Ensure adequate incubation condition for short-term or long-term treatment
- Pay attention to the precipitation of test compound
- Endpoint confluence 60%-80%
- Optional WuXi AppTec integrate services, e.g. FBS binding test, LC-MS concertation test, permeability test

- Standardized QC criteria: Z factor > 0.5, CV <15%
- Rich experience in data analysis and optimal parameters to fit the curve and EC50s determination
- Reference QC tracking

Economic Cell Panel Package

Economic cell panel packages provide a cost-effective cytotoxicity and efficacy study of your test articles on well-validated cell line matrix. The screening cell line packages are established by deep analysis of drug sensitivity, tumor genomics with RNA-Seq and encompassing large-scale cancer types. The service packages are diverse. You could choose the full-scale, common & rate or a more focused, tissue-specific cancer types panel according to your drug development process.

Service content and advantage

- Seeding density from cell growth curve
- Select from high quality cell banking system
- Growth Inhibition measured by ATP levels
- Automatic drug delivery system
- QC against Standard of Care (SoC)
- Flexible selection of cell line matrix
- Identifying sensitive and resistant cells
- Single drug or combination drug
- Cost saving
- Optional bioinformatics analysis for genotyping
- Integrated with in vivo CDX model

Panel#	Item	Cancer type#	Cell line#
1	Large scale of cancer type	50	210
2	Common cancer type	14	142
3	Rare cancer type	36	68
4	NSCLC focused	NSCLC	40~50
5	Other Lung cancer focused	Lung only	90~100
6	Breast cancer focused	Breast only	60~70
7	KRAS mutation 3D CTG	13	~70

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KRAS Mutant Panel Profiling



Types of KRAS mutation	Cell line #	CDX model #	RNA-Seq #
A146T	1	1	1
A146V	1	1	1
A18D	1	0	0
G12A	5	3	3
G12C	9	8	9
G12D	11	7	6
G12F	1	0	0
G12R	4	0	1
G12S	2	1	1
G12V	13	9	9
G13C	3	2	2
G13D	7	7	7
K117N	1	0	1
L19F	1	1	1
Q61H	3	3	2
Q61K	2	1	1
Q61L	2	2	1
Q61R	1	1	1
Wild Type (ampl)	1	1	1
Wild Type	1	0	1

CellTiter-Glo[®] 3D Cell Viability Assay principle



Compared with the 2D tumor model, the phenotype of cells in the 3D tumor model is closer to the expected results of oncogenes and tumor suppressors.

	CellTiter-Glo	CellTiter-Glo 3D
Applicable cell size	<350 μm	700 μm
lysis ability	++	+++++



Representative data of 3D-CTG with reference compound







- For screening of compounds targeting KRAS, 3D-CTG is more sensitive and suitable than 2D-CTG.
- Good sensitivity of 3D microtissues after comparing with different viability assays.
- Based on a simple model that effectively simulates tumor formation *in vitro*, ULA microtissues plate is utilized.

Customized Cell Panel Service

The screening is performed with **customized cell line panel** based on the nature of target and the specific question to be addressed.

Bioinformatics could assist selecting cell lines matrix and data analysis with specific genomic signature or mutation, as well as sensitive & resistant cancer types.

Customized cell screening tests can address numerous research questions throughout the discovery of anti-cancer drugs.



Case study: Olaparib Sensitivity Test in Different Cancer Cell Lines





Drug Combination Panel

Custom drug combination study

- Study combination drug responses to identify synergistic and antagonistic interactions with Combination Index (CI) calculation
- Flexibility in assay formats, dose range, and treatment times



Quantitative analysis demonstrated synergy of Compound X with ibrutinib, including at its lower dose.

Multi-omics Profiling by Bioinformatics Core

Our bioinformatics service is capable of discovering potential biomarkers related to drug response.

- Data analysis on multiple platforms (RNA-Seg/WGS/WES)
- Identification of the mode of action and suitable biomarkers
- 2000+ PDX models and cancer cell lines

(A) Mutation identified by WGS/WES

MDM2. TP53 • Associated with sensitivity 15 Associated with resistance -Log10(PValue) (PValue) DDB2 AC121757.2 ZMAT3 RRM2B AL031058.1 KLC3 VWA2 BAX LINC01357 SESN1 PLA2G4D BCI 2 USP45 MPP1 PPM10 -Log10 (\ZFP36 CDKN1A CCNG' GIGYF1 CCD₀₅₇ COG5 JAK2 \PARD3B DENND6B. OR2M2 KLK6 TTC37 AEBRIKRD26 TECRR MS4A8 ^AHSA1 -5.0 -2.5 0.0 25 -2 5.0 IC50 (geneMut - geneWT) Log2 Fold Difference (Resistant vs Sensitive)

(B) Differential gene expression in response to drug treatment by RNA-Seq





(C) Unsupervised hierarchical clustering of cells

with differential expression genes

- (A) Genetic feature profiling in a panel of 143 human cancer cell lines revealed that TP53 mutations strongly indicate cell resistance to Nutlin-3a, an MDM2 inhibitor.
- (B) Gene expression differential profiling for 97 cell lines showed that in addition to MDM2, a panel of genes (BCL2, BAX, DDB2, CDKN1A, CCNG1, RRM2B and PPM1D) associated with TP53 signaling pathway were downregulated, supporting the pivotal role of TP53 signaling pathway in Nutlin-3a efficacy.
- (C) Unsupervised hierarchical clustering 97 cancer cell lines using the differential expression genes from Panel (B) indicated that DLBCL cells seems to be more sensitive to Nutlin-3a treatment.



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For questions and requests, please email to OIU-BD-Translation@wuxiapptec.com



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