LIDE Translational Medicine Service Platform

OncoVee® MiniPDX ®

Shanghai LIDE

Shanghai LIDE Biotech, Co. Ltd.

Lab for **I**nnovated **D**iagnosis and **E**xperimental Therapeutics

Shanghai LIWEN

Jan 2023

Your LIDE Global Onboarding & Support Team

Josh Caggiula, VP
Global Client Relations
(Philadelphia, PA)

- Career foundation at J&J consumer and pharma businesses
- Led US operations for European-based omnichannel healthcare consultancy
- Partner and CMO/CCO for last 7 years at advanced life sciences IT and AI service provider

Kevin Zhang,
Global Study Coordinator
(Shanghai, China)

- Graduated from Syracuse University in the US with Master degree and majored in Biomedical engineering
- 2 years experience in Shanghai Tongji Hospital in China as a research assistant
- Study coordination and support for global LIDE team and LIDE's Study Directors in Shanghai & Xian

Loc Van, VP
Global Operations
(Charlotte, NC)

- Career foundation at J&J rotational leadership program
- Left J&J to focus on applications in growing digital landscape
- Last 10 years developing IT and digital infrastructure in pharma

Dr. Bo Peng,
Sr. Director, Biology Department
(Shanghai, China)

- Huazhong Agriculture University, Biology, Bachelor
- Huazhong Agriculture University, Preventive Veterinary Medicine, Master
- Zhejiang University, Cell biology, Doctorate
- 2013-2022: Technical Application Specialist, Manager, Thermo Fisher Scientific
- 2009-2013: R&D group leader, ChemPartner Inc.
- 2008-2009, R&D Scientist, Shanghai Genomic Inc.

LIDE's platform is a truly translational medicine operation

LIDE's foundation built around precision medicine in oncology

"BEDSIDE-TO-BENCH"

PERSONALIZED ONCOLOGY

LIWEN Biotech

LIWEN Diagnosis

LIYU Biotech

LILIN Tech

- *3000+ samples tested to date across 50 indications*
- *100+ Hospitals， 200+ PIs*
- *Investigator Initiated Trials (II-T)*

TRANSLATIONAL MEDICINE PLATFORM

"BENCH-TO-BEDSIDE"

ACCELERATED DRUG R&D

- *1777+ PDX*
- *70+ CDX*
- *100+ CR-PDO cell lines*
- *Humanized IO mouse models*
- *DNA RNA, Proteomics*
- *1800+ projects delivered*
- *270 clients worldwide*

To C

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aadlac INTERNATIONAL

To B

LIDE's spectrum of services

Functional Diagnostics

Target Identification/Validation

1. Pro-RNAi; shRNA
2. in vitro & in vivo CRISPR/Cas9

Pharmacology

1. 3D Spheroid TCA
2. CR Cell Lines
3. Organoid Assay
4. MiniPDX
5. CDX
6. PDX (drug resistant)
7. Orthotopic
8. Metastasis

Translational Medicine

1. MiniPDX Mouse Trial
2. Omic (DNA, RNA, Protein)
3. Flow Cytometry
4. IMC (Imaging Mass Cytometry)
5. Bioinformatics

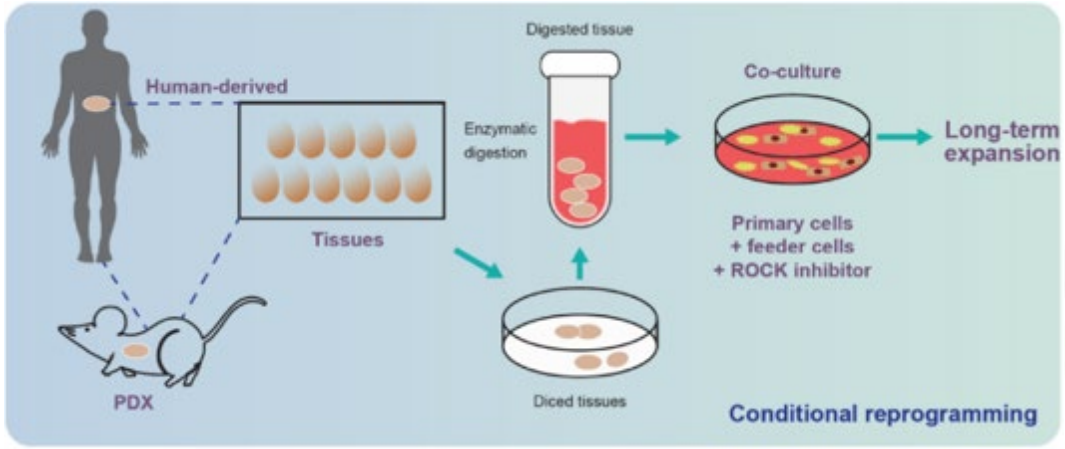
Clinical Biomarker

1. CAP Certified Pathology
2. Bioassays
3. Biomarker
4. PK for ADC
5. ADA Assay

1. Immuno-Oncology (T/B, NK, Mϕ, Dendritic)
2. Autoimmune-Inflammation models (Nephritis, Stroke)

In vitro: Conditionally Reprogrammed (CR) cells & organoids

1 CRC: Conditional Reprogrammed Cells

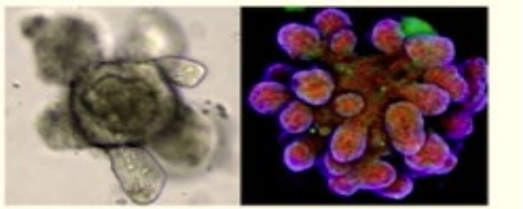


OncoBee™ 安可唯™

Sample Source	Tumor Type	#CRCs	Sample Source	Tumor Type	#CRCs
PDX	Lung cancer	12	Clinical Surgery	gallbladder carcinoma	4
	Breast Cancer	2		Cholangiocarcinoma	1
	Melanoma	1		Osteosarcoma	1
	Pancreatic Cancer	18		Glioma	3
	gastric Cancer	2		Intestinal Cancer	1
	Intestinal Cancer	1		Oral Squamous Cell Carcinoma	1
	Esophageal Cancer	4		lung Cancer	3
	Liver Cancer	14		Melanoma	1
	Cholangiocarcinoma	10		Oral Floor Carcinoma	1
	Glioma	4		Renal Cancer	2
	Osteosarcoma	1		Breast Cancer	1
Clinical Biopsy	Cardiac Cancer	1		Esophageal Cancer	1
	Colorectal Cancer	1		Ovarian Cancer	1
	Lung Cancer	2		Gastric Cancer	1
	Breast Cancer	1		Pancreatic Cancer	3
Clinical Puncture	Lung Cancer	2		Colorectal Cancer	1
	Malignant Thoracic Peritoneal Mesothelioma	1		Glioma	3
Clinical Hydrothorax	Lung Cancer	2			

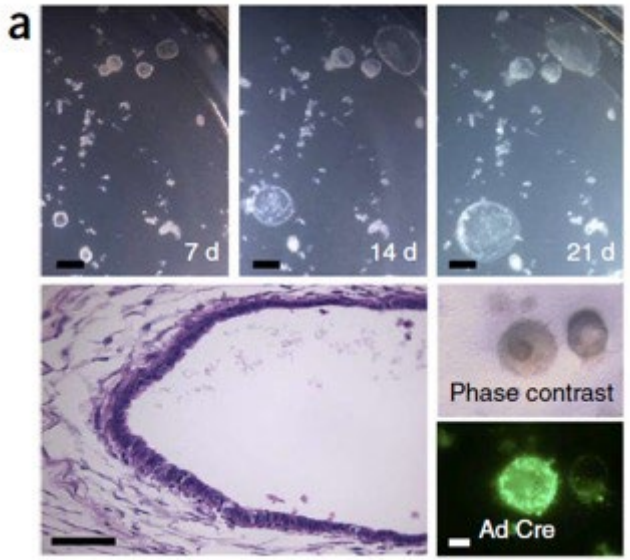
Available LIDE CR Cell Lines

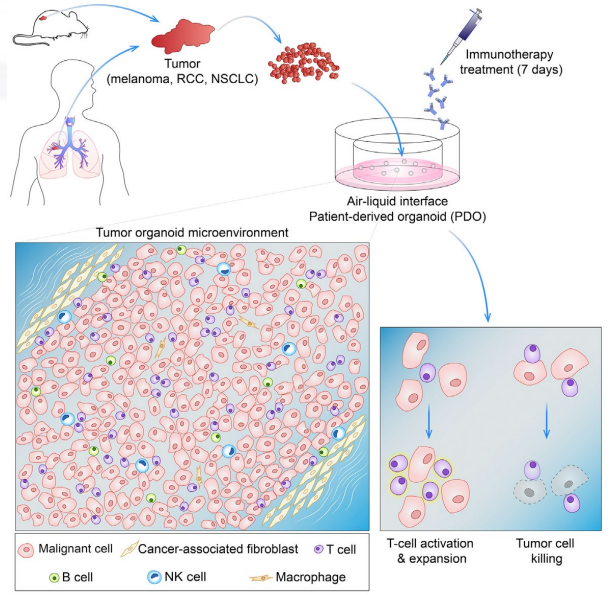
2 POD: Patient Derived Organoid Assay



Nat. Methods, 2018 Jan 3;15(1):24-26.
Imaging organoids: a bright future ahead.
Rios AC, Clevers H.

9June2021, Dr. Hans Clevers Visit LIDE





In vitro: 100+ Cell llines

Cancer	Cell line	Cancer	Cell line
Colon	Lovo,HT-29,Colo205,SW48,SW480,SW837, HCT-116,SW620,GP2D,RKO,SK-CO-1,DLD1, Colo 741	**Ovarian**	SK-OV-3, OVCAR-3, A2780, PA-1, ES-2, EFO-21, TOV-21G
Breast	MDA-MB-231, MDA-MB-468, HCC-1954, BT474, MDA-MB-157, MDA-MB-453, SK-BR-3, T-47D, MCF7	**Pancreatic**	MIA-Paca-2, Aspc-1, BXPC-3, HPAC, PANC-05.04, PANC-1, SW1990, Panc10.05, Capan 2
Gastric	MKN-45, NCI-N87, SNU-16, KATO III, KATO3-T5-BN, BGC823, SNU-5, NUGC4, MKN28, Hep3B, Hs746T	**Lung**	A549, CALU-1, H460, DMS14, H2009, H1975, H1703, HCC827, H2122, NCI-H226, Calu-3, H1299, H23, H358, SK-LU-1, EBC-1, H1993, H596, NCI-H441
Prostate	PC-3, LNCap, Du 145, 22RV1	**Osteosarcoma**	143B, MG-63, Saos-2, U-2 OS
Melanoma	A375, SK-MEL-5	**Esophageal**	KYSE30, OE19
Liver	HepG2, Hep-3B, Huh7, SNU-398, SK-HEP-1	**Glioblastoma**	U87MG, U251, A172, LN-229, U-118 MG
Lymphoma	Raji, Daudi, NALM-6, KARPAS-299, MV4-11, OCI-LY3	**AML**	MOLM-13, OCI-AML2
Leukemia/MM	K562, Jurkat	**Bladder Cancer**	5637
Fibrosarcoma	HT-1080	**Kidney**	A498
Epidermoid carcinoma	A431	**Cervical**	Hela
		Total	**106**

In vivo: 70 CDX models

Cancer type	Cell line	Quantity
Prostatic carcinoma	PC-3, 22Rv1, LNCaP, DU145	4
Malignant Melanoma	A375	1
Bladder cancer	T24, SW780	2
Breast cancer	MDA-MB-468, HCC-1954, MDA-MB-231,HCC1806, ZR-75-1,JIMT-1	6
Human epidermoid Carcinoma	A-431	1
Human Kidney Cancer	A-498, 786-O	2
Human embryonic kidney	HEK293-Claudin 18.2	1
Human cervical cancer	HeLa, C-33A	2
Liver cancer	Hep G2, Hep3B, SNU-398, Huh7	4
Fibrosarcoma	HT1080	1
Gastric carcinoma	KATO III, NCI-N87,BGC823,MKN45,N87-Claudin 18.2	5
Esophagus cancer	KYSE30	1
Pancreatic carcinoma	MIA PaCa-2 ,PANC-1,ASPC-1, BXPC-3	4
Lung cancer	NCI-H226,A549,Clau-3,NCI-H1975,SHP-77,NCI-H460,NCI-H2009,NCI-H2122,HCC827,NCI-H292	10
Leukemia/lymphoma	Raji, NALM6, MV-4-11, K-562, MOLT-4, OCI-LY3,Daudi, Ramos(RA 1)	8
Colorectal carcinoma	RKO, HCT-116, LOVO,SW620,COLO 205,HT-29,GP2D,SW480	8
Human ovarian carcinoma	SK-OV-3, PA-1,A2780	3
Brain glioma	U87-MG、U251	2
Myeloma	MOLP-8	1
Osteoblastoma	K7M2	1
Retinoblastoma	WERI-Rb-1, Y-79	2
Human oral squamous	SCC090	1

In vivo: LIDE's 1777+, variant-rich PDX model library

Summary: LIDE's PDX library is continually updated from samples from our clinical work. Currently over 1777 models, covering 40+ cancer types, variant rich covering popular expression targets, rare mutations or drug resistance.

Benefit: LIDE PDX models cover some hard-to-find, naturally occurring cancer profiles to support 2nd line drug development or drugs targeting rare cancers.

Cancer Type	Resistant To:	Rare Specific Genetic Alteration(s)	
NSCLC	Eriotinib Osimertinib Crizotinib Brigatinib Anti PD-L1 ab	**EGFR:** exon19del/T790M/L858R/exon20ins/C797S **ALK:** EML4-ALK/L1196M **Cmet:** ampli/exon14ski/CD47-MET **RET:** KIF5B-RET	**ROS1:** CD74-ROS1/G2032R **KRAS:** G12C **PTEN:** Y68X **P13K:** E726K
Breast Cancer	CDK4/6i	**TNBC/ER+**	
Multiple Myeloma	Bortezomib	**CD47+/CD38+**	
Cholangiocarcinoma	Paclitaxel	**KRAS:** G12C	**FGFR:** BICC1-FGFR2
Colorectal Cancer	Avastin	**KRAS:** G12C	**BRAF**: V600E
Hematological Malignancy	Rituximab Imatinib	/	
Gastric Cancer	Herceptin	**HER2:** ampli	**KRAS:** G12C
Brain Cancer	/	**EGFR:** VIII	**cMET:** PTPRZ1-MET
Melanoma	Anti PD-1 ab	**BRAF:** V600E	
Ovarian Cancer	Platinum PARPi	/	

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Cancer Type	PDX
Adenoid cystic carcinoma (ACC)	5
Bladder cancer	5
Breast cancer	44
Cervical cancer	47
Cholangiocarcinoma	81
Chordoma	2
Colon cancer	113
Duodenal carcinoma	15
Endometrial cancer	17
Esophageal cancer	41
Fallopian tube carcinoma	2
Gallbladder carcinoma	36
Gastric cancer	200
Gastrointestinal stromal tumor	6
Brain cancer	69
Hepatocellular carcinoma	103
Hepatoblastoma	41
Head and neck cancer	7
Lung cancer	156
Lymphoma	16
Mucinous carcinoma	5
Mediastinal endoblastoid sinus tumor	1
Malignant mesothelioma	2
Melanoma	4
Neuroendocrine tumor	6
Osteosarcoma	58
Ovarian cancer	200
Paget's Disease	1
Pancreatic cancer	305
Periampullary carcinoma	2
Penile cancer	2
Prostate cancer	7
Rectal Cancer	80
Renal carcinoma	9
Sarcoma	38
Extramedullary tumor	1
Spleen cancer	1
Acute lymphoblastic leukemia	10
Acute myelocytic leukemia	16
Chronic Lymphocytic Leukemia	2
Multiple Myeloma	3
Urethral carcinoma	4
Unknown origin tumor	14
Totol	1777

TKI Drug resistant/gene alteration PDX models

Cancer Type	Model ID	PDX Tumor Pathology	PDX SOC validation: resistant to	Gene alterations		PDX matching CR Cell line	
				Gene	mutation or fusion	Yes or no	Highest Passage
NSCLC	LD1-0025-200717	Poorly - Moderately differentiated adenocarcinoma	Erlotinib Osimertinib	EGFR	19del (746-750) T790M C797S	Yes	P12+12
	LD1-0025-200730	poorly differentiated adenocarcinoma	Erlotinib Osimertinib	EGFR c-met CDK4	L858R amplification amplification	Yes	P6
	LD1-0025-360961	Moderately differentiated adenocarcinoma	Erlotinib Osimertinib	EGFR CDKN2A	19del (746-750) deletion	No	-
	LD1-0025-200662	adenocarcinoma	Erlotinib Osimertinib	EGFR c-met	19del (748-753) over-expression	No	-
	LD1-0025-361336	Moderately - highly differentiated squamous cell carcinoma	Osimertinib Erlotinib	EGFR c-met PIK3CA	19del (746-750) amplification C901F mutation	No	-
	LD1-0025-215676	adenocarcinoma	Erlotinib	EGFR CDKN2A	L858R T790M deletion	Yes	P12+5
	LD1-0025-217655	Poorly - Moderately differentiated adenocarcinoma	Erlotinib	EGFR	19del (746-750)	No	-
	LD1-0025-200713	Poorly differentiated adenosquamous carcinoma	Erlotinib	EGFR CCND1 CDK4	L858R amplification amplification	No	-
	LD1-0025-200739	Poorly - Moderately differentiated adenocarcinoma	Erlotinib Osimertinib	EGFR PIK3CA	19del (747-751) H1047L mutation	No	-
	LD1-0025-390637	adenocarcinoma	Crizotinib	ALK	EML4-ALK fusion; L1196M mutation	No	-
	LD1-0025-361019	Poorly - Moderately differentiated adenocarcinoma	Crizotinib Brigatinib	ROS1 CDKN2A	CD74-ROS1 fusion G2032R mutation deletion	No	-

Drug resistant/gene alteration PDX models

Cancer Type	Model ID	PDX Tumor Pathology	PDX efficacy SOC validation	Gene alterations		PDX matching CR Cell line	
				Gene	mutation or fusion	Yes or no	Highest Passage
NSCLC	LD1-0025-360715	squamous cell carcinoma	LOXO292 sensitive	RET	KIF5B-RET fusion	Yes	P10+11
	LD1-0025-361384	poorly differentiated adenocarcinoma	-	RET	KIF5B-RET fusion	No	-
	LD1-0006-215625	adenocarcinoma	Crizotinib sensitive	ALK	EML4-ALK	Yes	P16+3
	LD1-0006-215648	adenocarcinoma	Crizotinib sensitive	ALK	EML4-ALK	No	-
	LD1-0025-360815	Poorly differentiated adenosquamous carcinoma	-	ALK	EML4-ALK	No	-
	LD1-0025-360807	poorly differentiated adenocarcinoma	Capmatinib sensitive	MET	exon14 skipping	No	-
	LD1-0025-361333	Poorly differentiated adenocarcinoma	-	MET	CD47-MET fusion	No	-
Glioblastoma	LD1-0020-361404	Diffuse midline glioma	-	MET	PTPRZ1-MET fusion	No	-
				H3-3A	K27M		
Glioblastoma	LD1-0020-200624	Glioblastoma	-	EGFR	EGFRVIII mutation	No	-
				PIK3CA	G118D		
Lung cancer	LD1-0025-361646	Poorly - Moderately differentiated adenocarcinoma		KRAS	G12C	Yes	P5
				YES1	amplification		
Gastric cancer	LD1-0017-200636	Poorly - Moderately differentiated adenocarcinoma	5-FU and Cisplatin	KRAS	G12C	No	-
Cholangiocarcinoma	LD1-0060-200791	intrahepatic cholangiocarcinoma	-	KRAS	G12C	Yes	P15+11
Rectal cancer	LD1-0038-200642	Moderately differentiated adenocarcinoma	-	KRAS	G12C	No	-
	LD1-2038-200906	Highly differentiated tubular adenocarcinoma	-	KRAS	G12C	No	-
				SMARCB1	R377C		
Colon cancer	LD2-0012-200830	mucinous adenocarcinoma	-	BRAF	V600E	No	-
				RAD50	R1239X		
Breast cancer	LD2-0009-200825	Malignant spindle cell tumor	-	TNBC：HER2(-)ER(-)PR(-)		No	-
	LD2-0009-200827	poorly differentiated adenocarcinoma	-	TNBC：HER2(-)ER(-)PR(-)		No	-

Targeted drug resistant PDX models

Cancer Type	Model ID	PDX Tumor Pathology	PDX SOC validation: resistant to	Gene alterations		PDX matching CR Cell line	
				Gene	mutation or fusion	Yes or no	Highest Passage
Gastric cancer	LD1-2017-361443	Poorly - Moderately differentiated adenocarcinoma	Herceptin resistant	Her2	+++(IHC)	No	-
				EGFR	T790M		
Ovarian cancer	LD1-0032-361588	adenocarcinoma	Olaparib resistant	RAD51D	p.Lys91Ilefs*13	No	-
	LD1-2032-200962	Poorly - Moderately differentiated adenocarcinoma	Olaparib resistant	BRCA1	p.N408Cfs*5	No	-
	LD1-0032-200876	serous adenocarcinoma	Olaparib resistant	BRCA1	p.N1015Pfs*5	No	-
	LD1-0032-362878	Poorly differentiated adenocarcinoma	Olaparib resistant	BRCA1	p.N1015Pfs*5	No	-
Breast cancer	LD1-0009-362383	Invasive breast carcinoma, grade	Palbociclib resistant	ER+		Yes	P3+3
Breast cancer	LD1-2009-362153	Invasive breast carcinoma, grade 3	Abemaciclib resistant	-	-	No	-
Breast cancer	LD1-2009-361973	Invasive breast carcinoma, grade 3	Palbociclib resistant	PIK3CA	E545K	No	-
Colon cancer	LD1-0012-361016	Moderately differentiated adenocarcinoma	Avastin resistant			No	-
DLBCL	LD2-6026-200614	CLL Richter syndrome Diffused large B cell lymphoma	Rituximab resistant	SF3B1	K666T	No	-
				ERBB2	S310F		
Cholangiocarcinoma	LD1-0011-200770	Intrahepatic bile duct adenocarcinoma	Paclitaxel	FGFR2	BICC1--FGFR2 fusion	No	-
Multiple myeloma	LD1-0006-370728	multiple myeloma	Bortezomib + Dexamethasone	CD47+CD38+（FACS）		No	-
				KRAS	Q61H		

PD-1/PD-L1drug resistant PDX models

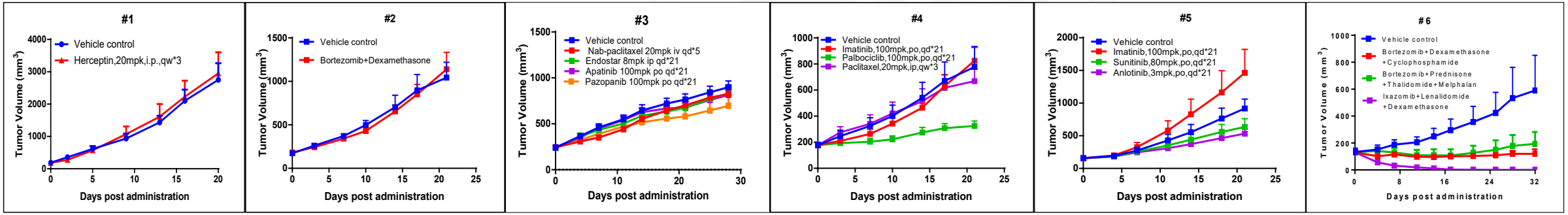
Cancer Type	Model ID	PDX Tumor Pathology	PDX SOC validation: resistant to	Gene alterations	
				Gene	mutation or fusion
NSCLC	LD1-0025-200756	Poorly differentiated adenocarcinoma	anti-PD-L1 ab	-	-
	LD1-0025-390663	Moderately differentiated adenocarcinoma	anti-PD-1 ab	-	-
	LD1-0025-361384	Poorly differentiated adenocarcinoma	anti-PD-1 ab	RET	KIF5B-RET fusion
	LD1-0025-362118	NSCLC	anti-PD-1 ab	ERBB2	20ins (G776delinsVC)
	LD1-0025-200794	SCLC	anti-PD-1 Ab	-	-
Melanoma	LD1-0024-362394	melanoma	anti-PD-1 Ab	BRAF	V600E
cervical cancer	LD1-0010-362343	Nonkeratinizing Squamous Cell Carcinoma	anti-PD-1 Ab	-	-
Breast cancer	LD1-0009-362391	Grade 3 invasive breast cancer	anti-PD-1 ab	KRAS	G12C
Breast cancer	LD1-0009-362585	Grade 3 invasive breast cancer	anti-PD-1 ab		
Ovarian cancer	LD1-2032-200962	Poorly differentiated adenocarcinoma	anti-PD-1 ab	BRCA1	p.N408Cfs*5
Colorectal Liver metastases	LD1-2038-362000	Poorly - Moderately differentiated adenocarcinoma	anti-PD-1 Ab	KRAS	G12D
leiomyosarcoma	LD1-0036-362497	leiomyosarcoma	anti-PD-1 Ab		
Ovarian cancer	LD1-0032-362851	High-grade serous carcinoma	anti-PD-1 Ab	-	-
Ileocecal tumor	LD1-2013-362125	Poorly differentiated adenocarcinoma	anti-PD-1 Ab		
Tongue cancer (head and neck tumor)	LD1-2023-411020	High- moderately differentiated squamous cell carcinoma	anti-PD-1 Ab		
NSCLC	LD1-0025-215621	adenocarcinoma	PD1-Ab Resistant Patients-Hyper Progressive Disease	MDM2	amplification
NSCLC	LD1-0025-217643	adenocarcinoma	PD1-Ab Resistant Patients-Hyper Progressive Disease	MDM2	amplification

No.	PDX_ID	Cancer_type	Gene_symbol	Expression		Copy number	
				TPM	Note	CN	Note
1	LD1-0025-215621	Lung cancer	MDM2	1114.92	over-expression	26	amplification
2	LD1-0025-217643	Lung cancer	MDM2	407.59	over-expression	12	amplification
3	LD2-0011-202117	Cholangiocarcinoma	MDM2	281.52	over-expression	9	suggestive amp
4	LD1-0032-200711	Ovarian cancer	MDM2	110.87	up-regulated	9	suggestive amp
5	LD1-0032-362826	Ovarian cancer	MDM2	132.3	up-regulated	7	suggestive amp
6	LD5-0024-362077	Melanoma	MDM2	130.86	up-regulated	6	suggestive amp

No.	PDX_ID	Cancer_type	gene_symbol	function_class	transcripts	aa_changes
1	LD1-0010-200614	Cervical cancer	DNMT3A	frameshift	ENST00000321117	p.V60fs
2	LD1-0025-360662	Lung cancer	DNMT3A	Splicing/insertion of 22 AAs	ENST00000321117	c.1668-1G>A
3	LD1-0011-200943	HCC	DNMT3A	frameshift	ENST00000321117	p.A610fs
4	LD1-0011-200699	HCC	DNMT3A	Splicing	ENST00000321117	c.2174-2A>T
5	LD1-0040-361280	AML	DNMT3A	nonsynonymous SNV	ENST00000321117	p.R882P
6	LD1-0040-362740	AML	DNMT3A	nonsynonymous SNV	ENST00000321117	p.R882H

Most models verified against clinical history

Model ID	Clinical Diagnosis	Clinical Treatment(s)
#1	Gastric adenocarcinoma	Herceptin Resistant
#2	Multiple myeloma	Bortezomib+Dexamethasone Resistant
#3	Osteosarcoma	Paclitaxol/Endostar/Apatinib/Pazopanib Resistant
#4	Malignant melanoma	Imatinib/Paclitaxol Resistant Palbociclib Sensitive
#5	GIST	Imatinib Resistant Sunitinib/Anlotinib Sensitive
#6	Multiple myeloma	Bortezomib+Dexamethasone+Cyclophosphamide Sensitive Bortezomib+Prednisone+Thalidomide+Melphalan Sensitive Ixazomib+Lenalidomide+Dexamethasone Sensitive



- Efficacy data in PDX models established using biopsy from corresponding patients demonstrated consistent responses with their clinical treatment(s).

LIDE Typical engagement workflow

Overview

1. Review LIDE platform
2. Identify models of interest
3. Discuss study needs
4. Understand areas of interest

1 week

Consultation

1. Sign NDAs
2. Schedule deep-dives with lead science team
3. Align study expectations
4. Draft study design and quote

2-3 Weeks

Study Preparation

1. Sign MSAs
2. Initiate study (first invoice)
3. Coordinate shipping and/or ordering
4. Revive models
5. Implant mice

1-2 Months

Initiate Study

1. Assign Study Director
2. Finalize study protocol
3. Start study and begin weekly study updates

1-2 Months

Application of the Highest Industry Standards

International Lab and Research Standards

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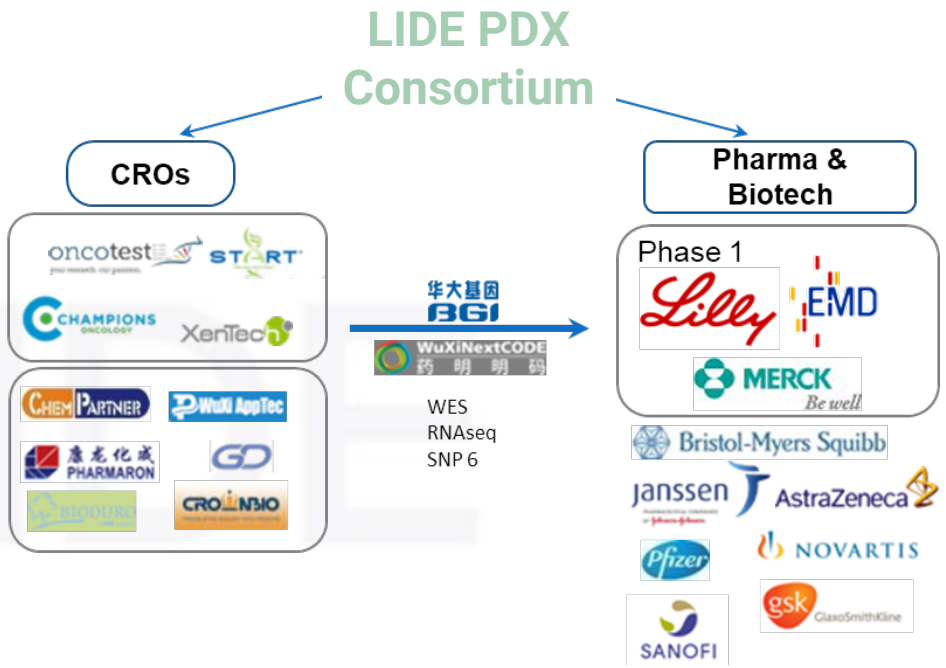
Setting PDX Standards in China



Chinese Government Issued Certifications





Performance across 11+ years, 200+ clients, 1700 projects

NA & EU

CHINA

ACADEMIC