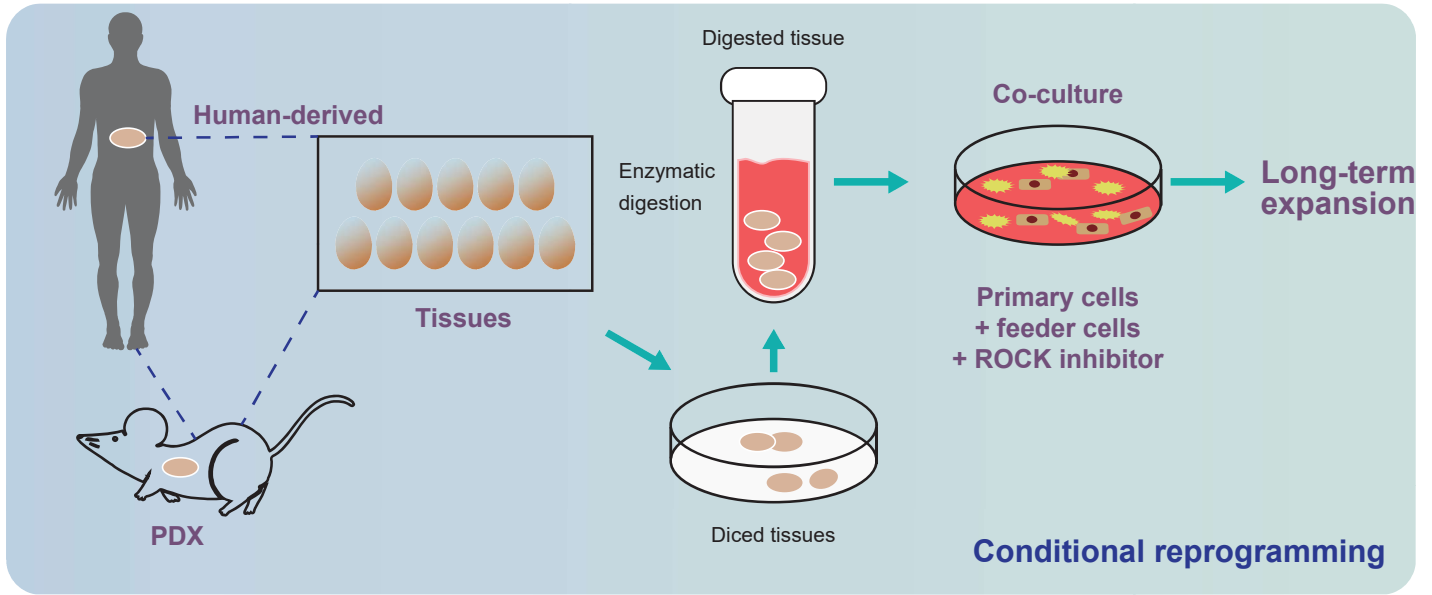


1 CR (Conditional Reprogramming) Overview

Conditional reprogramming (CR) emerges as a novel tool for long-term culture of primary epithelium cells derived from almost all origins without alteration of genetic background of primary cells. It is demonstrated that no more than 5% of primary tumors can be expanded in vitro for a long term previously, CR successfully enables generation of cell lines from almost 90% of tissue specimens from human normal and tumor origins, which maintains both intratumor and intertumor heterogeneity. CR shows broad prospects in application to varied areas including disease modeling, drug evaluation, drug discovery as well as precision medicine.



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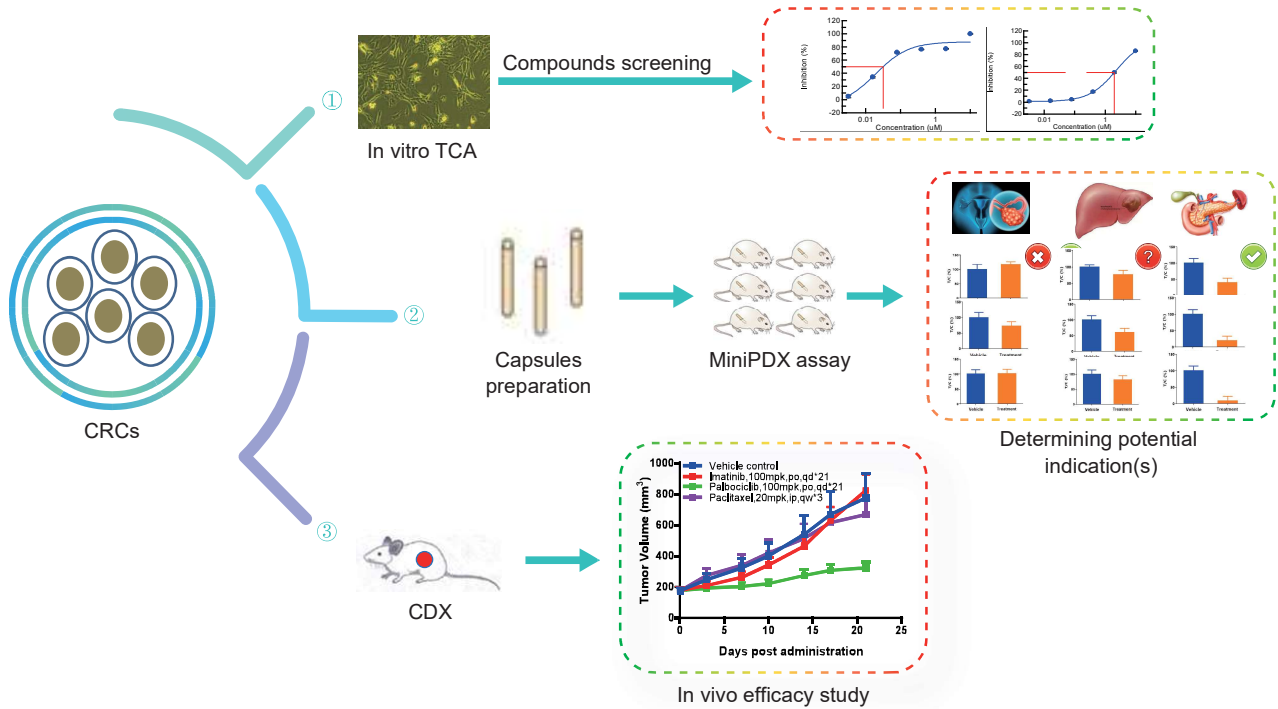
LIDE has developed over 100 CR cells (CRCs, left), in which some of PDX matching CRCs exert special drug resistance/genetic alteration (right).

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
Clinical Biopsy	Cardiac Cancer	1		Breast Cancer	1
	Colorectal Cancer	1		Esophageal Cancer	1
	Lung Cancer	2		Ovarian Cancer	1
Clinical Puncture	Breast Cancer	1		Gastric Cancer	1
	Lung Cancer	2		Pancreatic Cancer	3
Clinical Hydrothorax	Malignant Thoracic Peritoneal Mesothelioma	1		Colorectal Cancer	1
	Lung Cancer	2		Glioma	3

Tumor Type	Drug Resistance	Gene Alteration
NSCLC	Erlotinib	EGFR: exon19del/L858R/T790M/C797S
	Osimertinib	
	Cetuximab	
	EAI045	
	Cetuximab+EAI045	
BC	Primary CDK4/6 Inhibitor	KIF5B-RET fusion
Melanoma	Paclitaxel	ROS1: ROS1-RILPL2-MAP3K5-ROS1 fusion

2 Application of CRCs in Preclinical R&D

As its intratumor and intertumor heterogeneity, CRCs can be a substitute for commercialized cancer cell lines for ① in vitro TCA compounds screening; ② potential indication screening via MiniPDX assay; and ③ in vivo efficacy study using CRCs generated CDX.



3 Application of CRCs in Target Identification

Pro-siRNA can be applied for high-throughput screening of potential unknown target(s) from established CRCs with specific drug resistance and/or genetic alteration, while targeted therapy using generated inhibitor or antibody can be further developed as investigated new drug candidates.

