# Developing 3-D Organoids
for an Advanced Platform of Precision Oncology

Hyunsook Lee

Seoul National University

Early-onset Chromosome instability in Brca2-knockout MEFs

Lee et al,. *Mol. Cell* (1999)
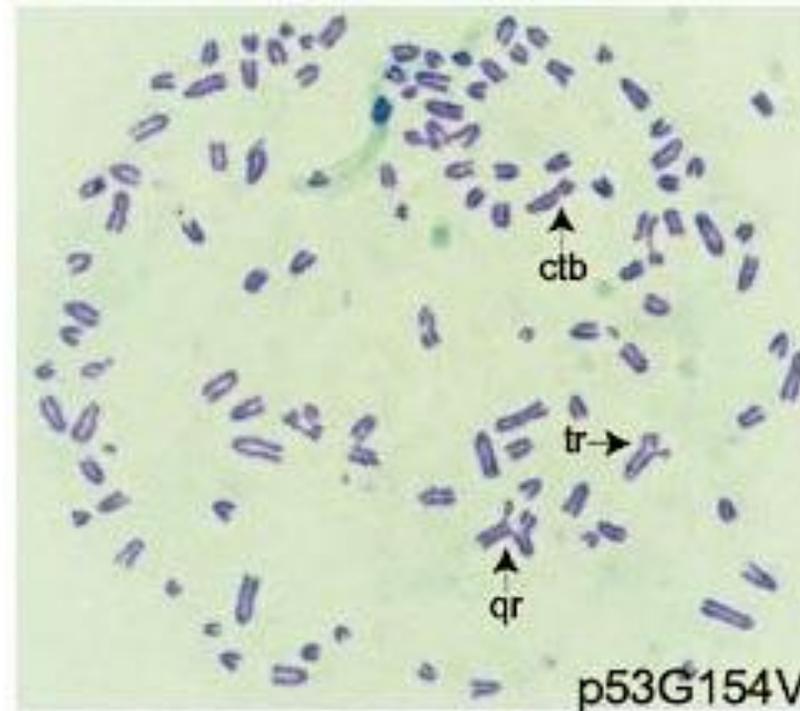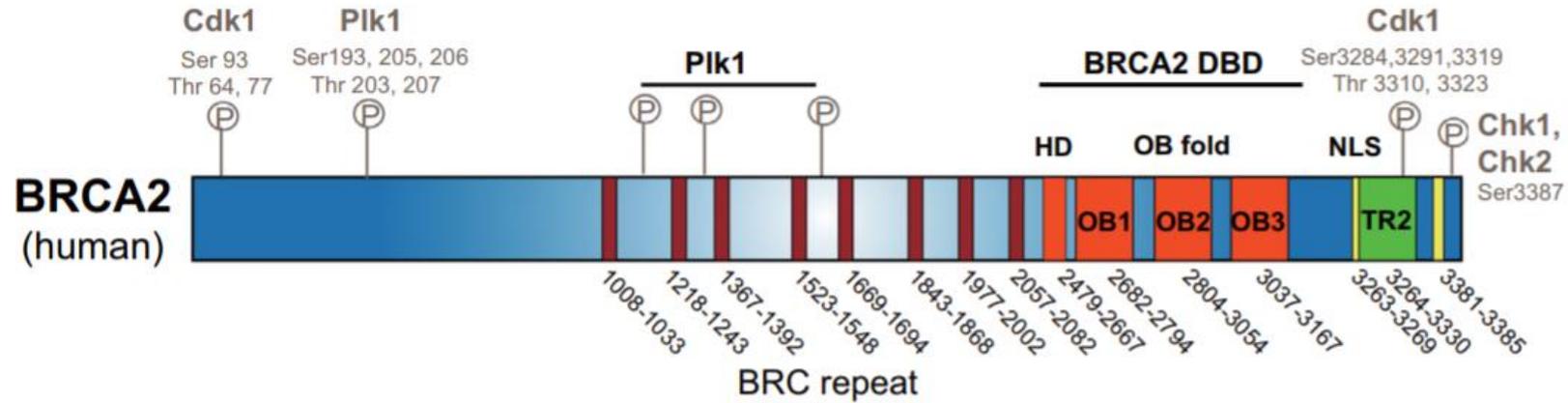
Development of 3-D organoid cultures as a novel ex vivo system for disease modeling
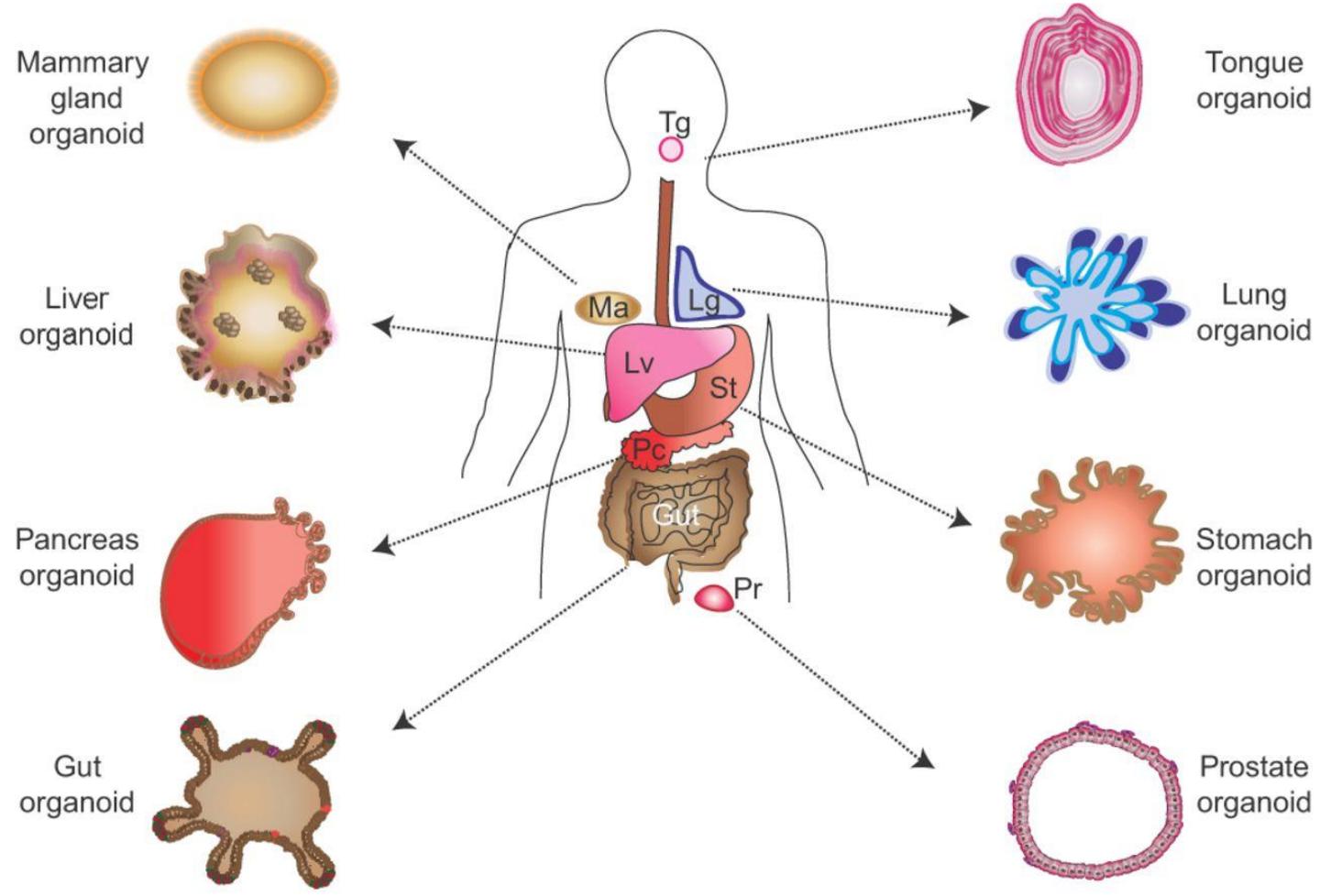
- CONTENTS -
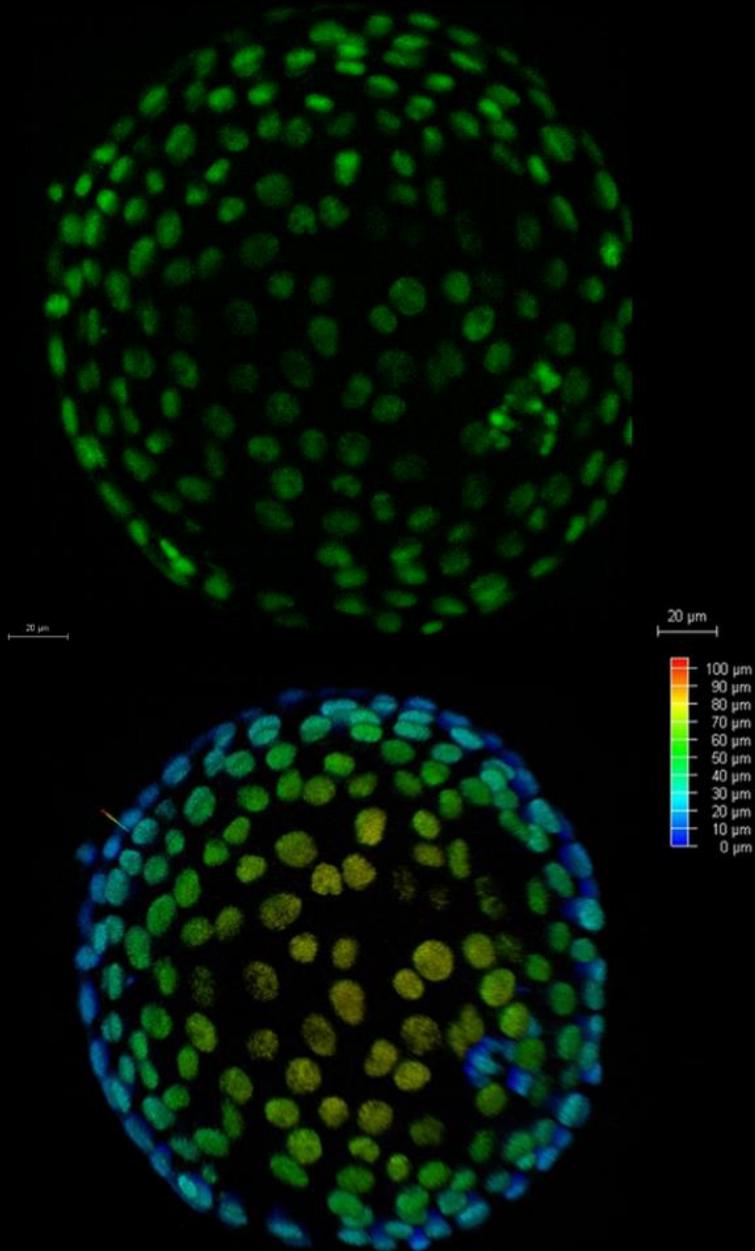
Pancreatic Cancer is the most lethal disease

➜ Modeling is essential!
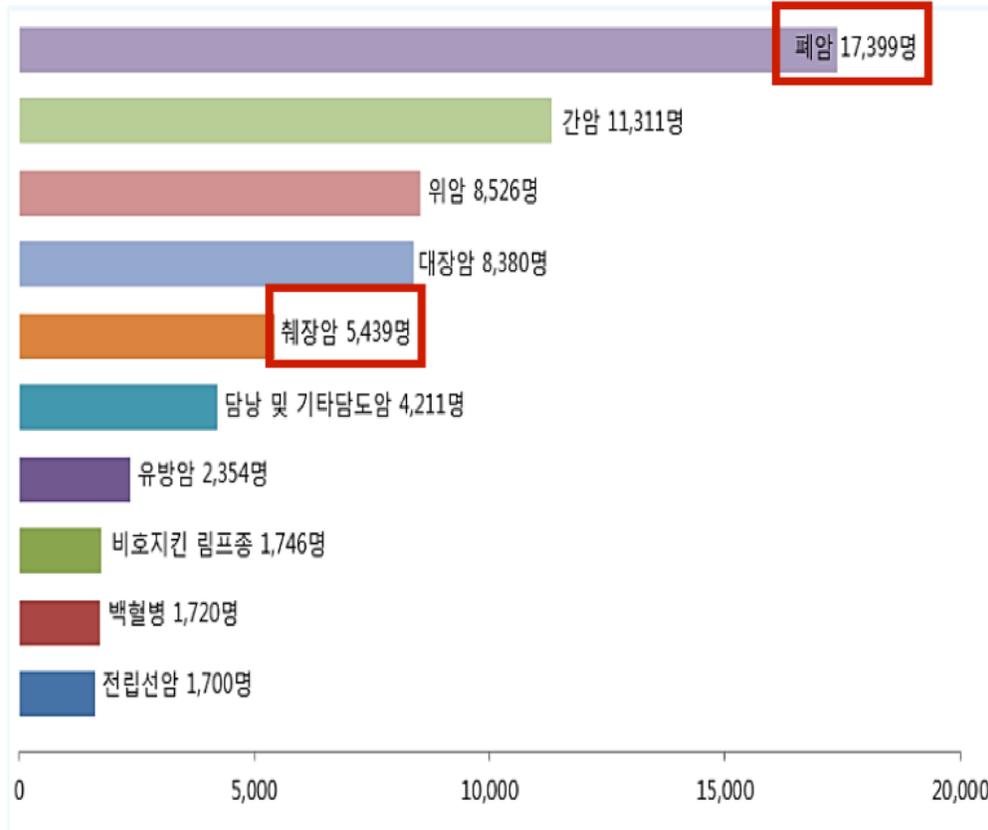
▲ 2015년 암종별 사망자수 (출처:국가암정보센터)

| Rank	Site	Summary Stage							
		Localized		Regional		Distant		Unknown	
		%	5-year survival	%	5-year survival	%	5-year survival	%	5-year survival
	All Cancers	**43.8**	**89.0**	**30.9**	**72.7**	**16.3**	**19.7**	**9.0**	**54.0**
1	Thyroid	43.0	100.6	49.6	100.4	0.7	71.8	6.8	99.2
2	Stomach	58.8	95.5	23.6	59.0	11.3	5.8	6.3	44.3
3	Colon and rectum	38.2	95.3	40.6	80.4	14.7	19.0	6.5	59.8
4	Lung	19.4	58.2	26.7	31.8	44.1	5.4	9.8	16.6
5	Breast	56.6	97.9	34.8	90.2	4.8	36.8	3.8	83.1
6	Liver	45.5	51.6	24.7	17.6	15.7	2.8	14.1	23.4
7	Prostate	56.8	100.6	21.8	95.7	9.0	38.6	12.4	87.6
8	Pancreas	10.6	29.7	31.6	13.6	45.6	1.7	12.2	10.4
9	Gallbladder etc.	24.4	51.3	40.0	34.6	24.0	2.5	11.6	18.6
10	Non-Hodgkin lymphoma	40.2	80.7	13.4	68.5	33.7	53.5	12.7	68.1

▲ 2009~2013년 암종별, 병기별 5년 생존율
(출처:국가암정보센터)

# Patient-derived organoid culture from fine needle biopsy (FNB)
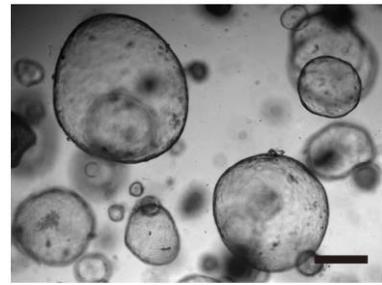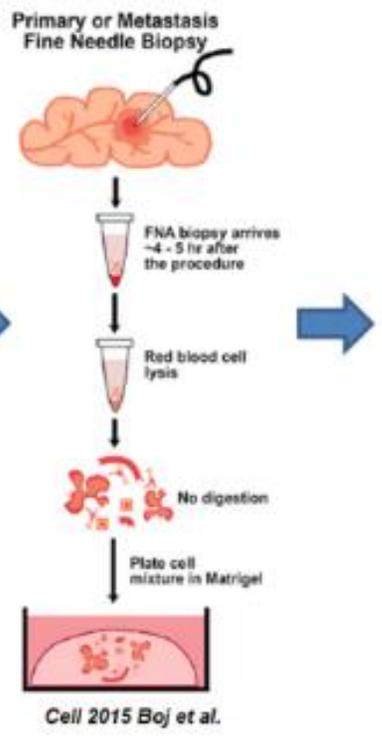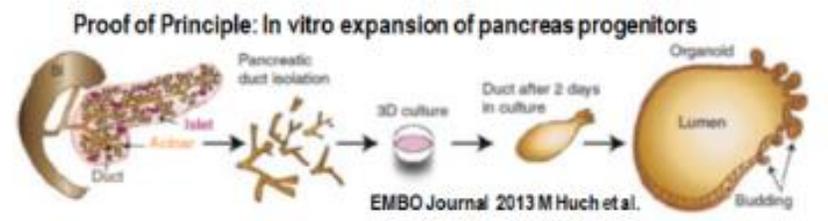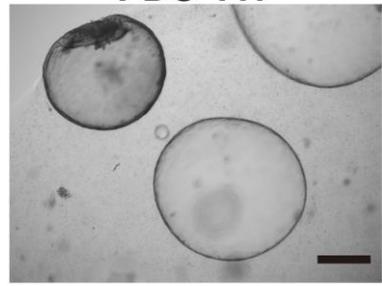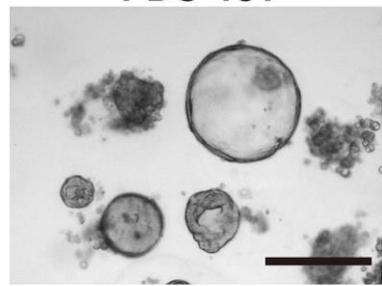
Validation of Patient-Derived Organoids
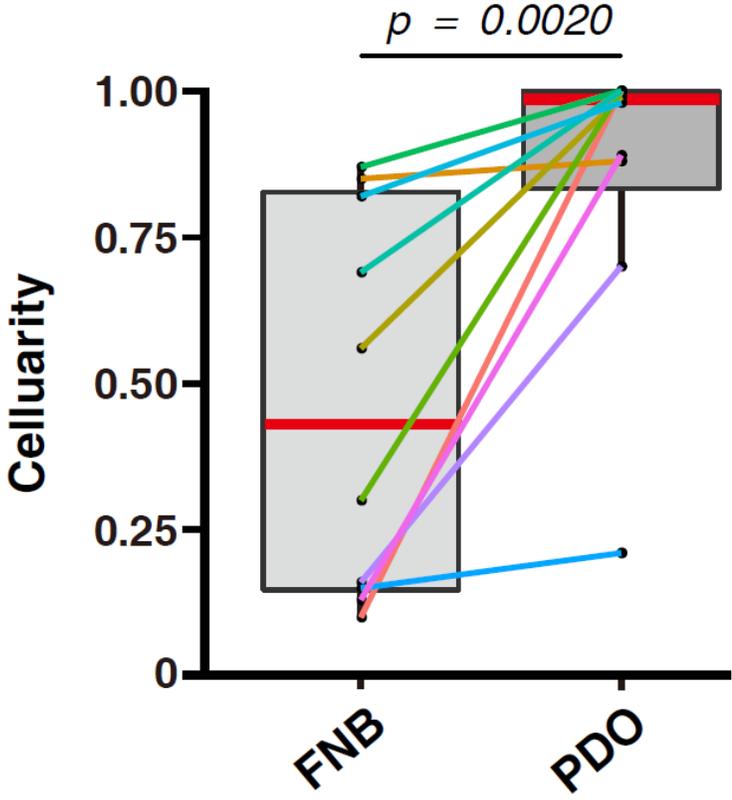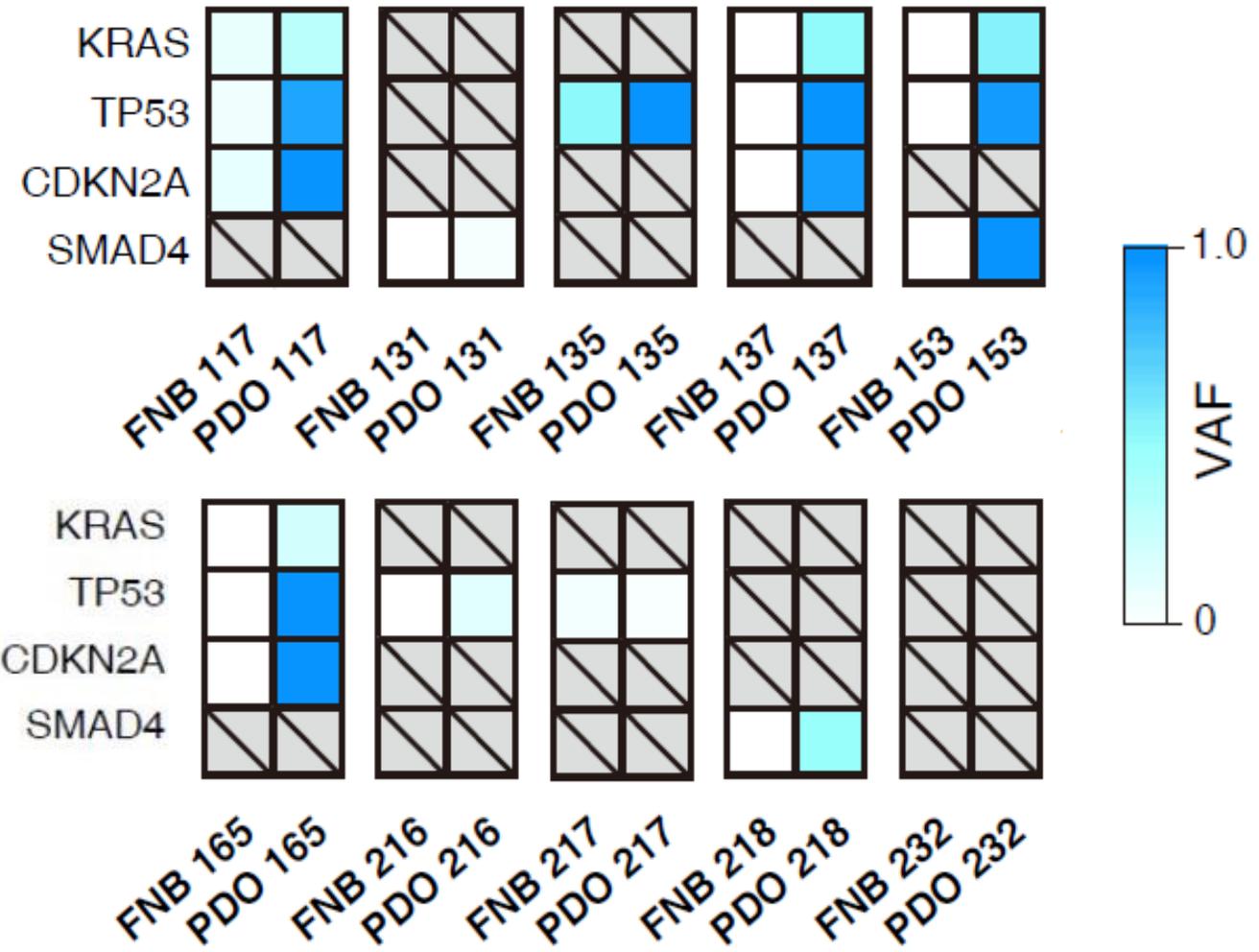
# Application of Organoids in Precision Medicine and Drug Repositioning
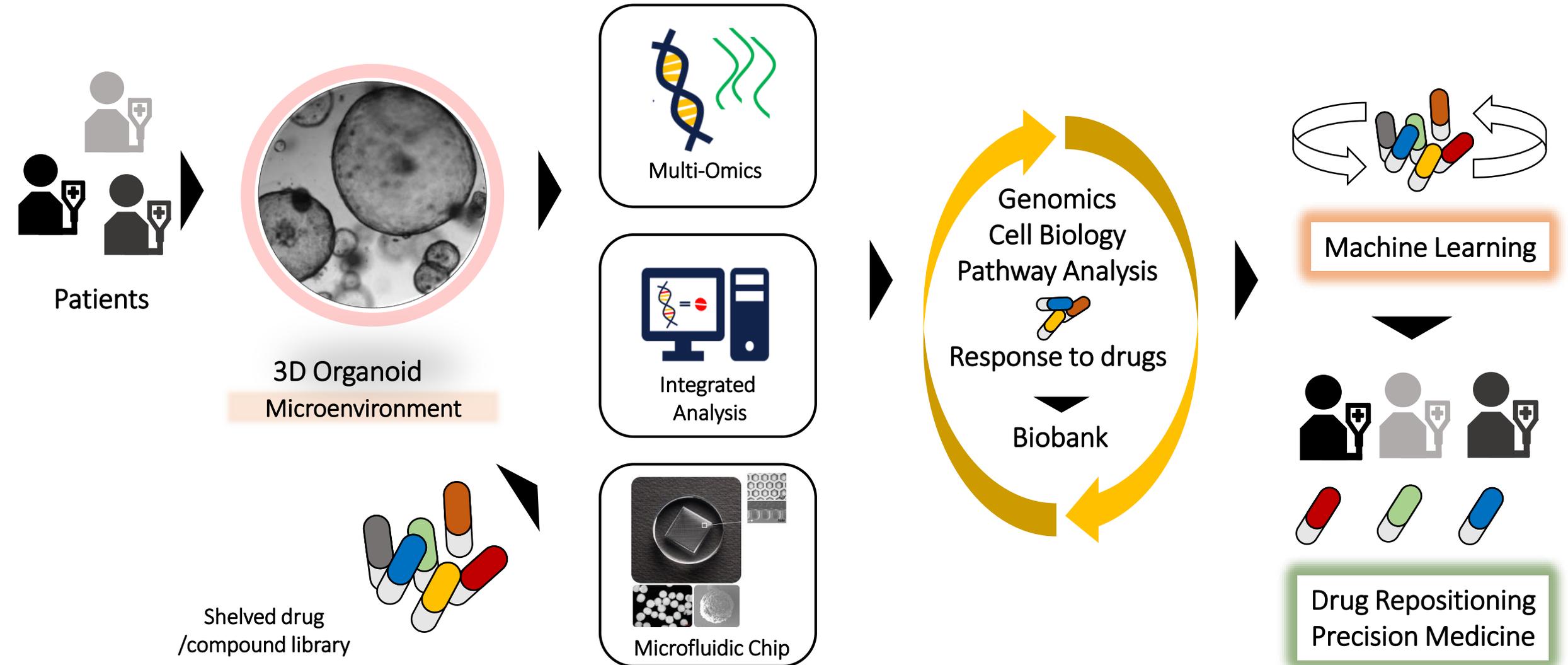
# Targeting BRCA2-deficiency using genetically modified mouse organoids
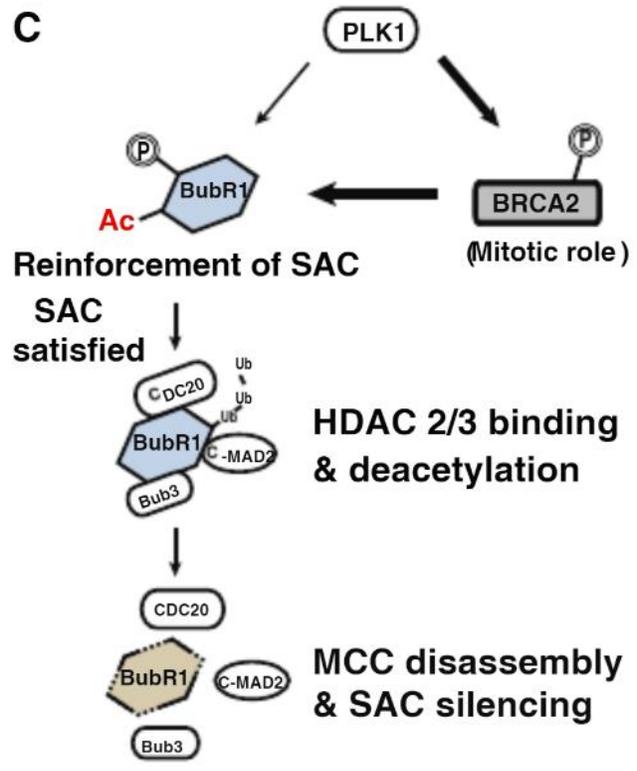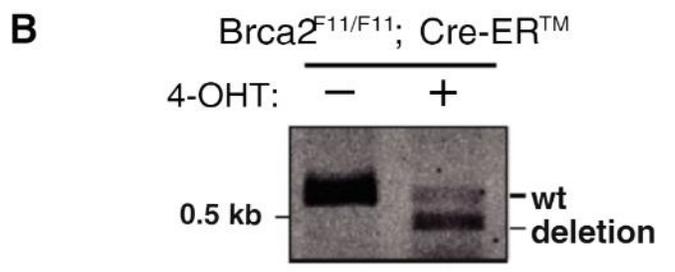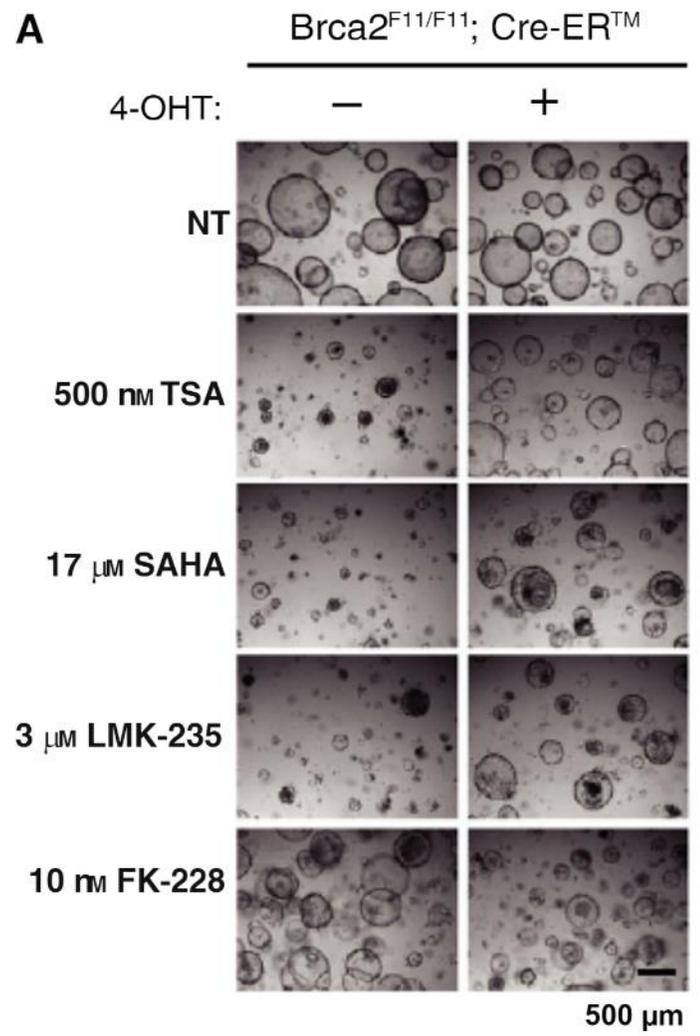
# Induction of ALT after BRCA2 depletion in telomerase-null mice
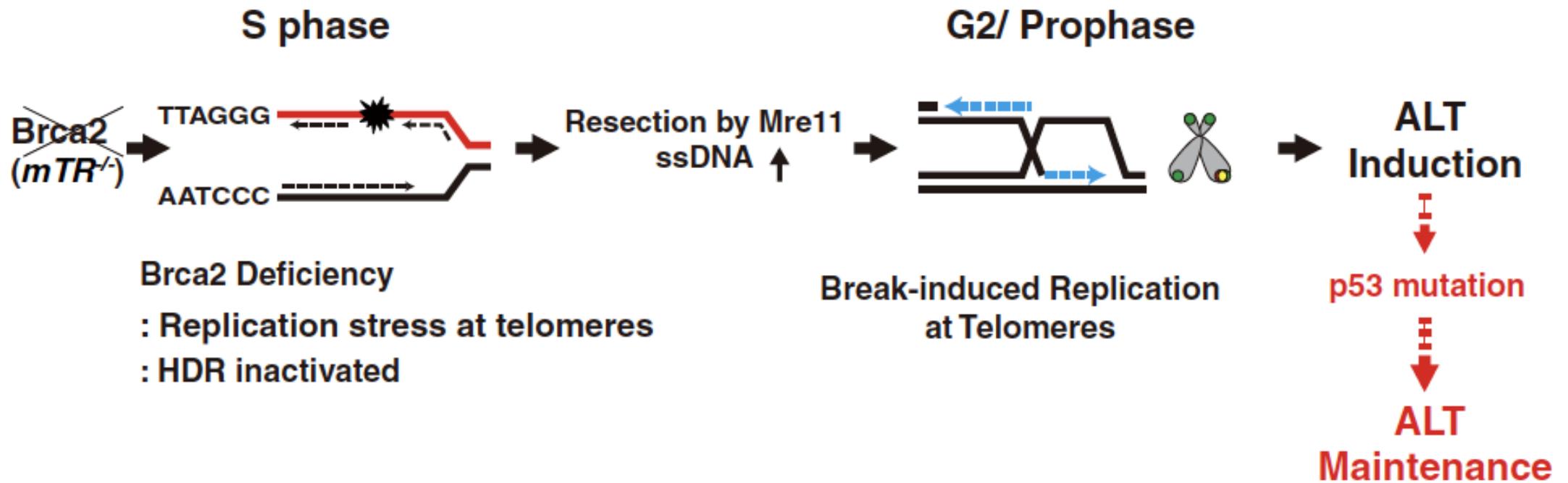
# Modeling different types of Pancreatic disease

ALT cancer Model

TP 53 knockout Model

Kwon et al., The FEBS J. (2019); patented 2021
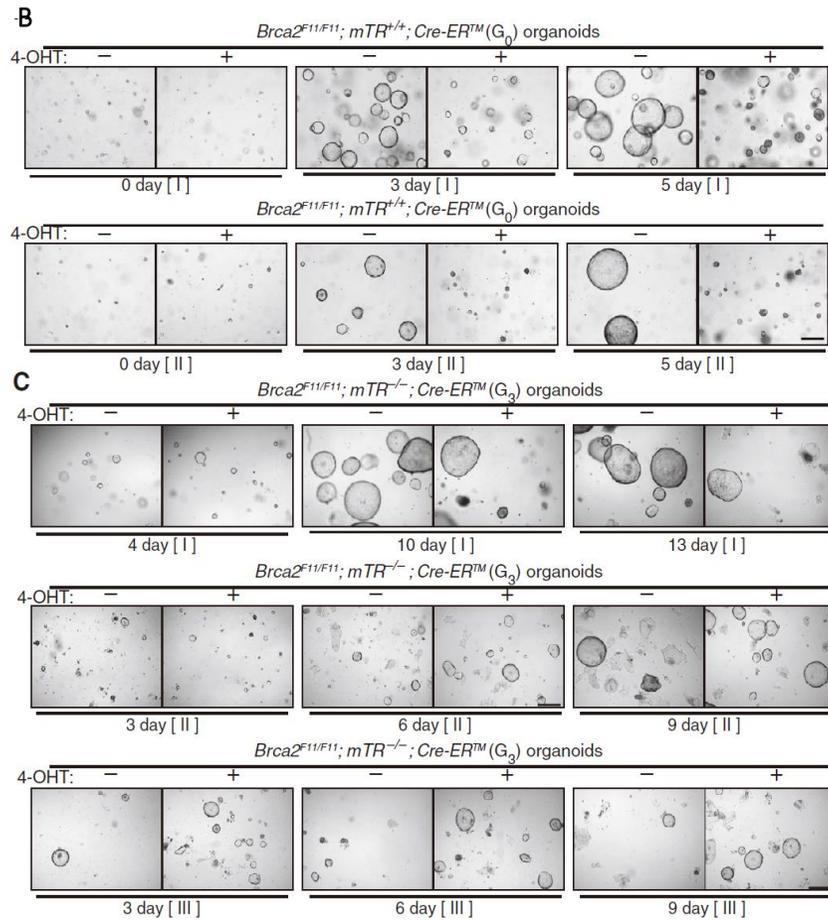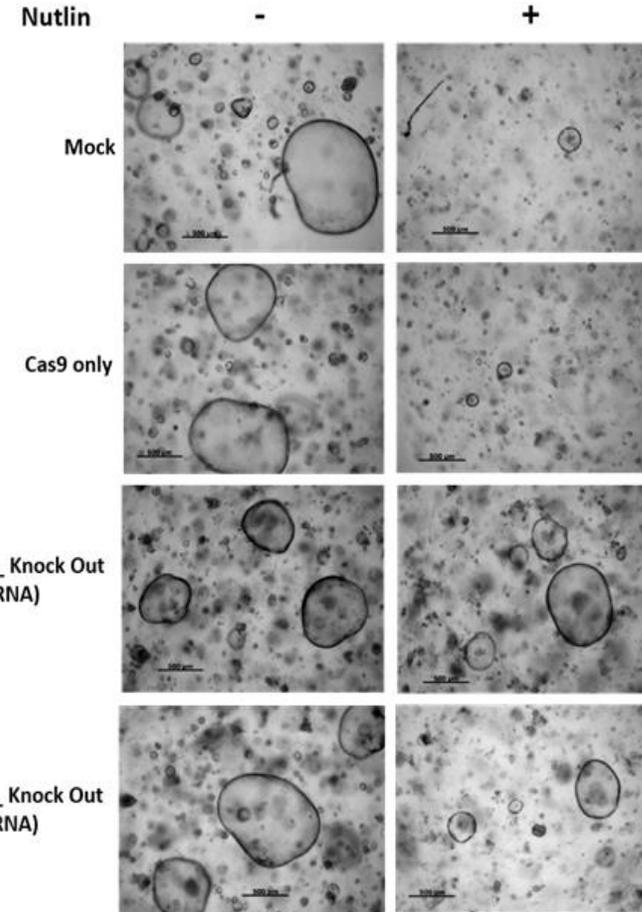
Establishment of Matrigel Free Organoid-on-chip Culture
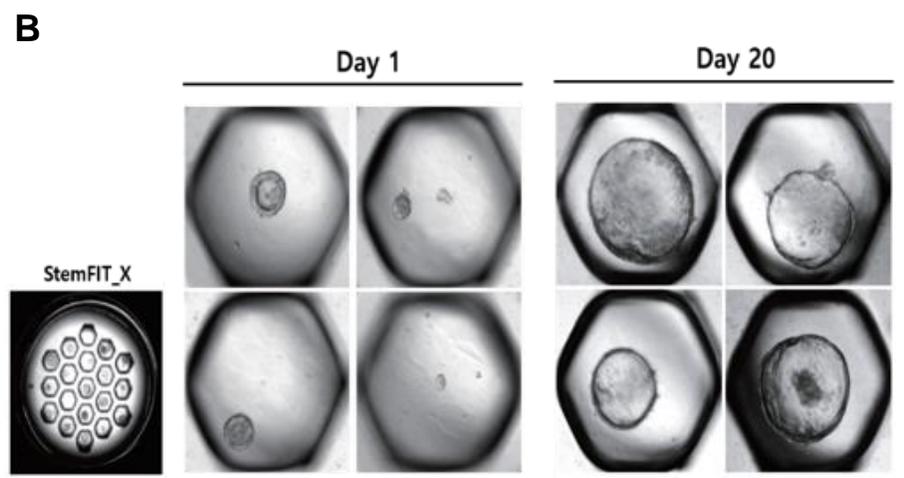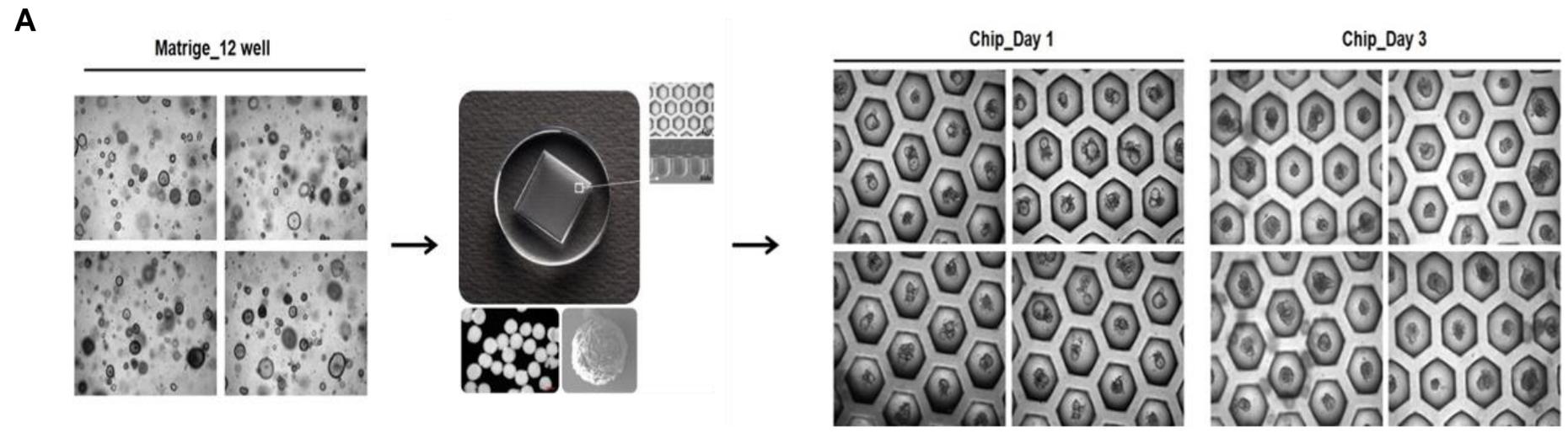
Developing organoid cultures using microfluidic chip for highthroughput screening
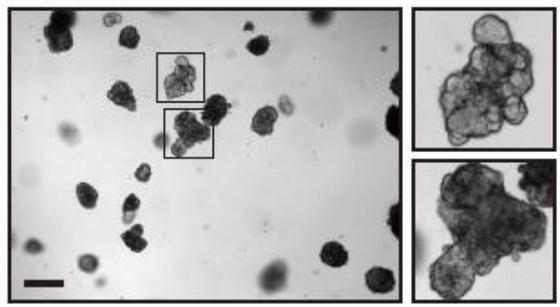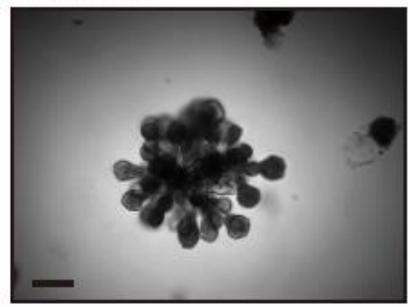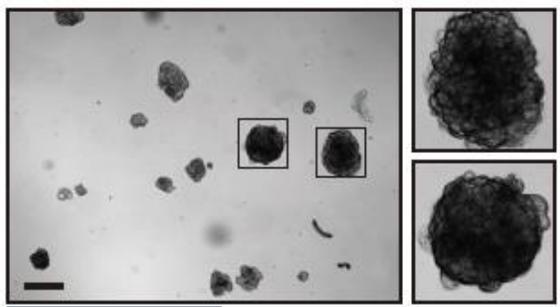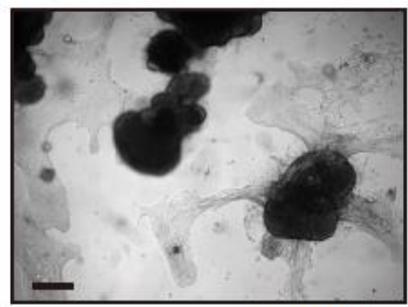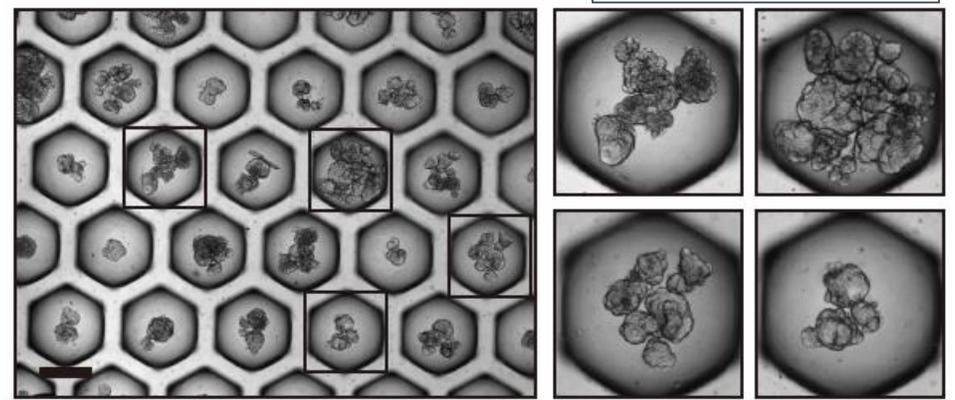

*Triple Negative Breast Cancer (TNBC) Organoid cultures from Surgical samples*

Validation of TNBC organoids
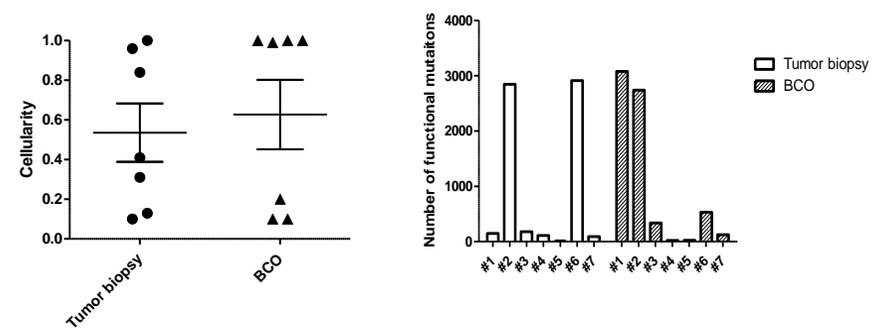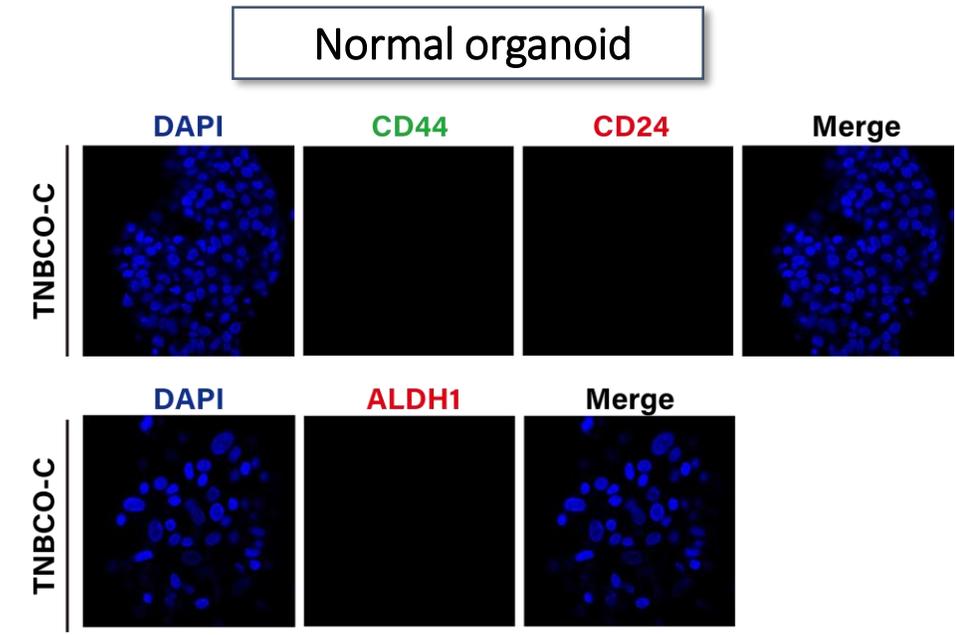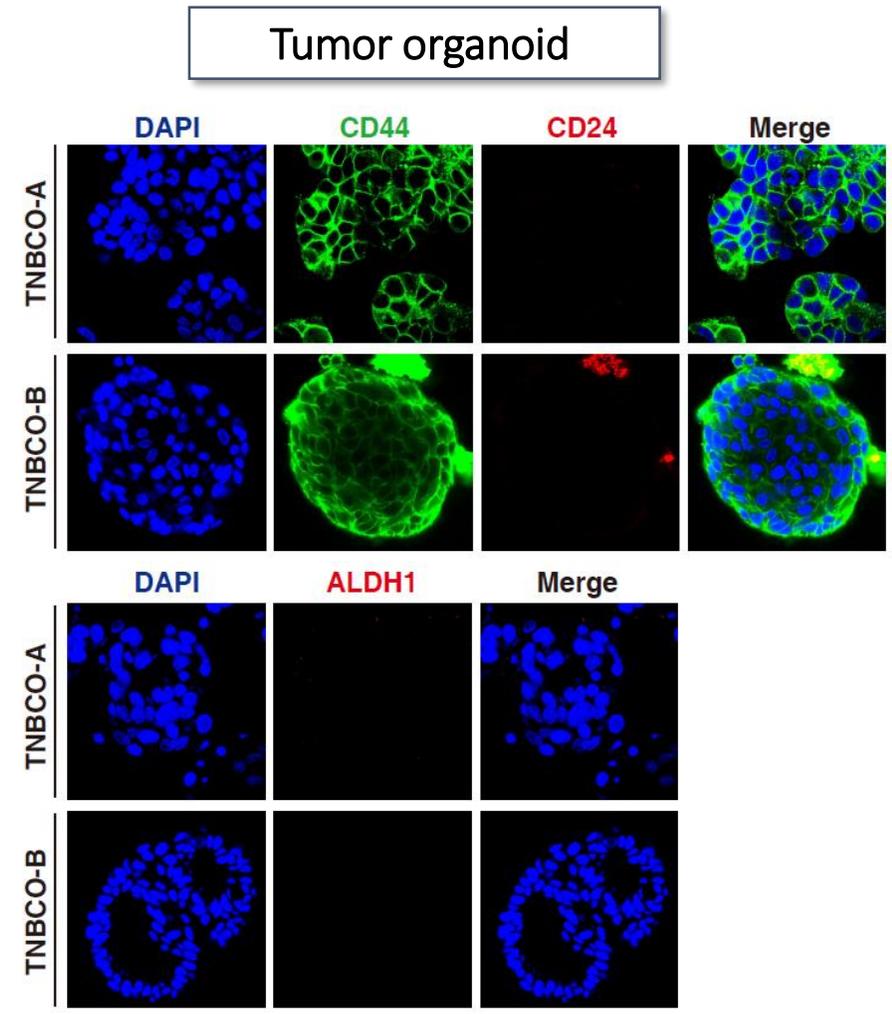
3-D Kras$^{G12D/+}$ Mouse Organoids for the validation of Anti-Cancer Drug Activity of RN
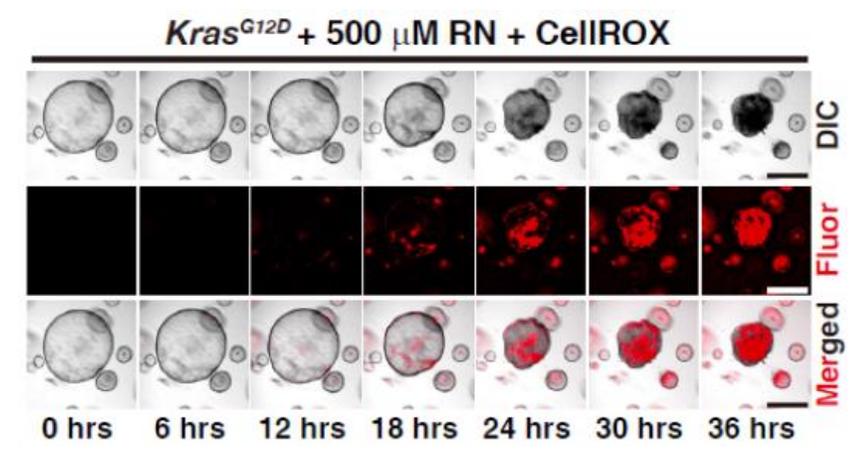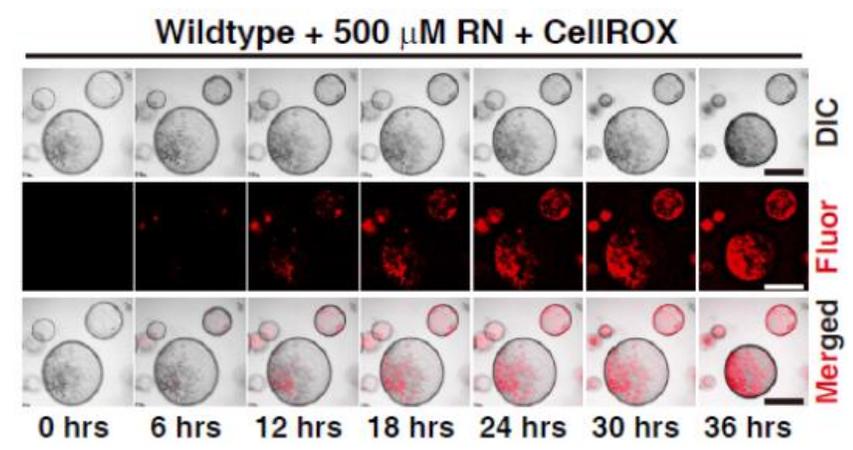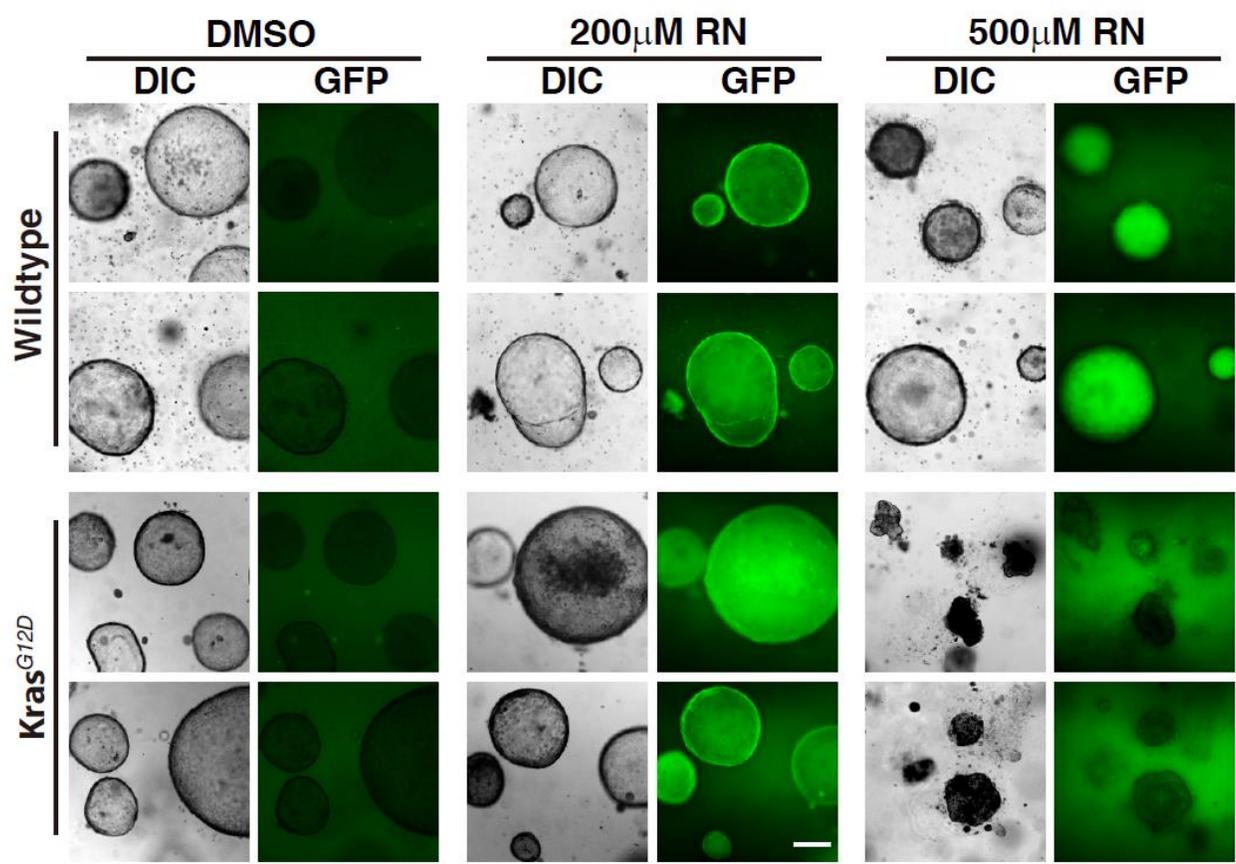
Anti-Cancer activity of RN in Patient-derived Organoids (PDOs)

*PDO: Patient Derived Organoid

|			
RN (μM)	0	100	200	500
Gemcitabine (μM)	0	1	2.5	5
TSA (nM)	0	100	200	500
SAHA (mM)	0	5	10	25
LMK-235 (μM)	0	10	25	50
BI2536 (nM)	0	10	25	50
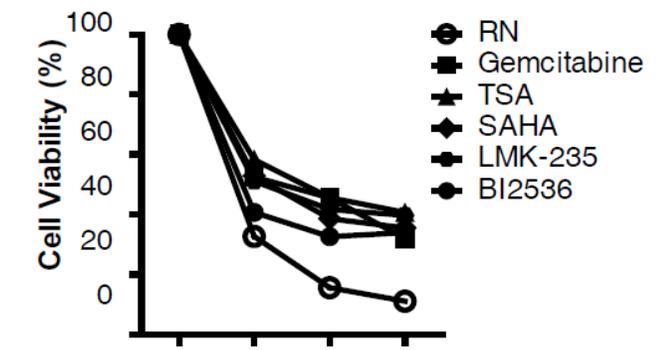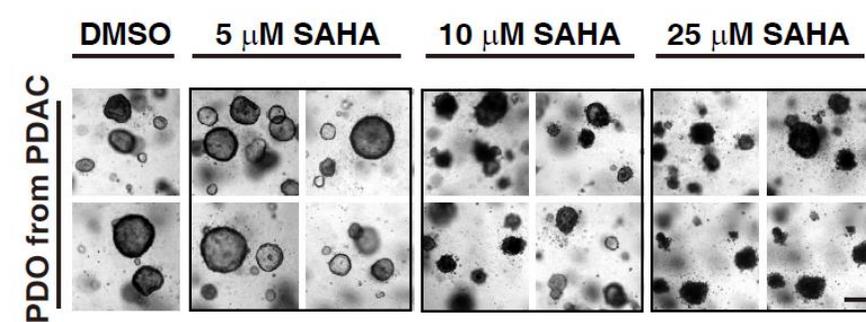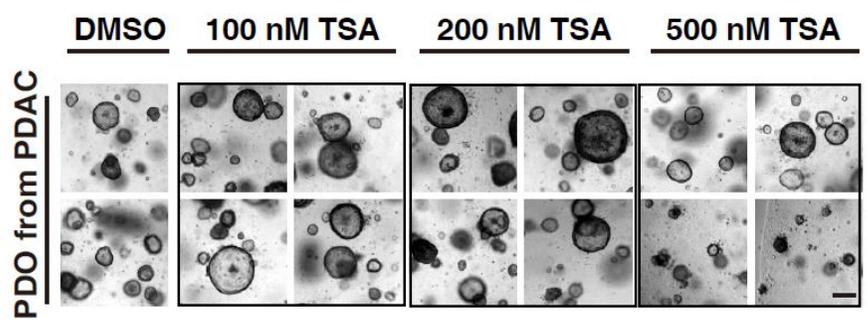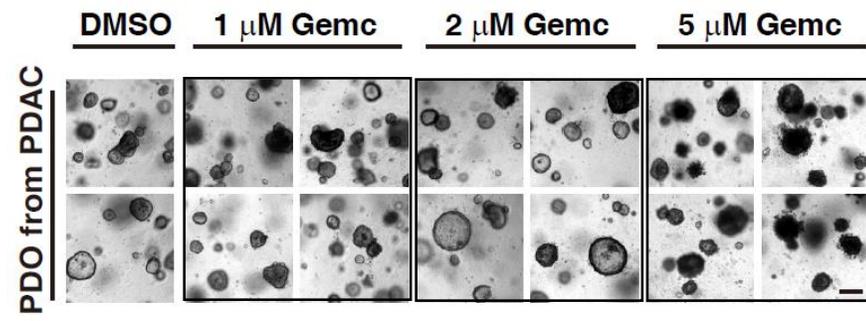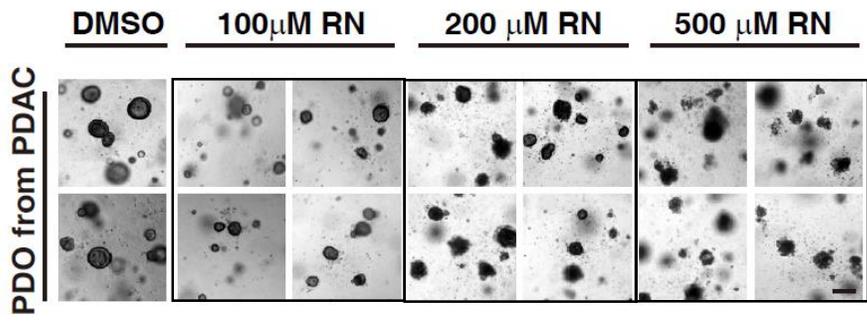
*Drug concentrations as indicated

manuscript in preparation

Drug Test Platform with PDOs using Organoid-on-chip

*PDO: Patient Derived Organoid
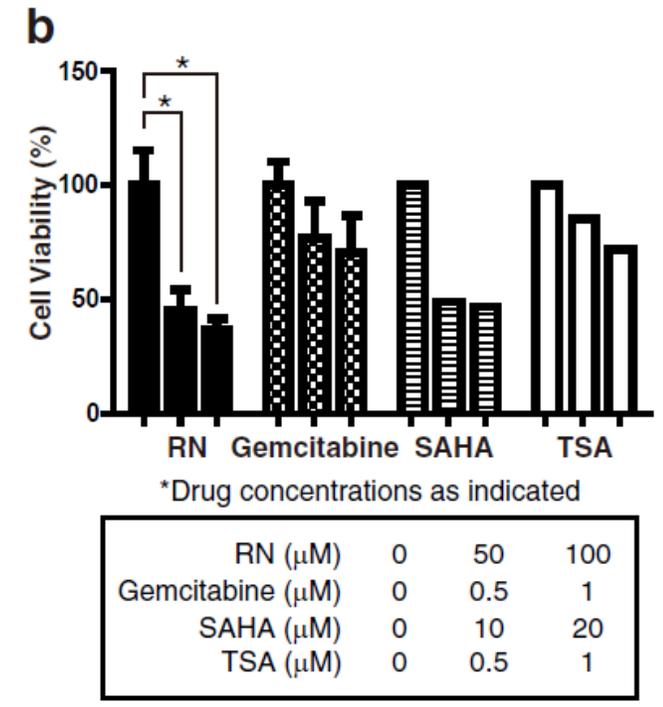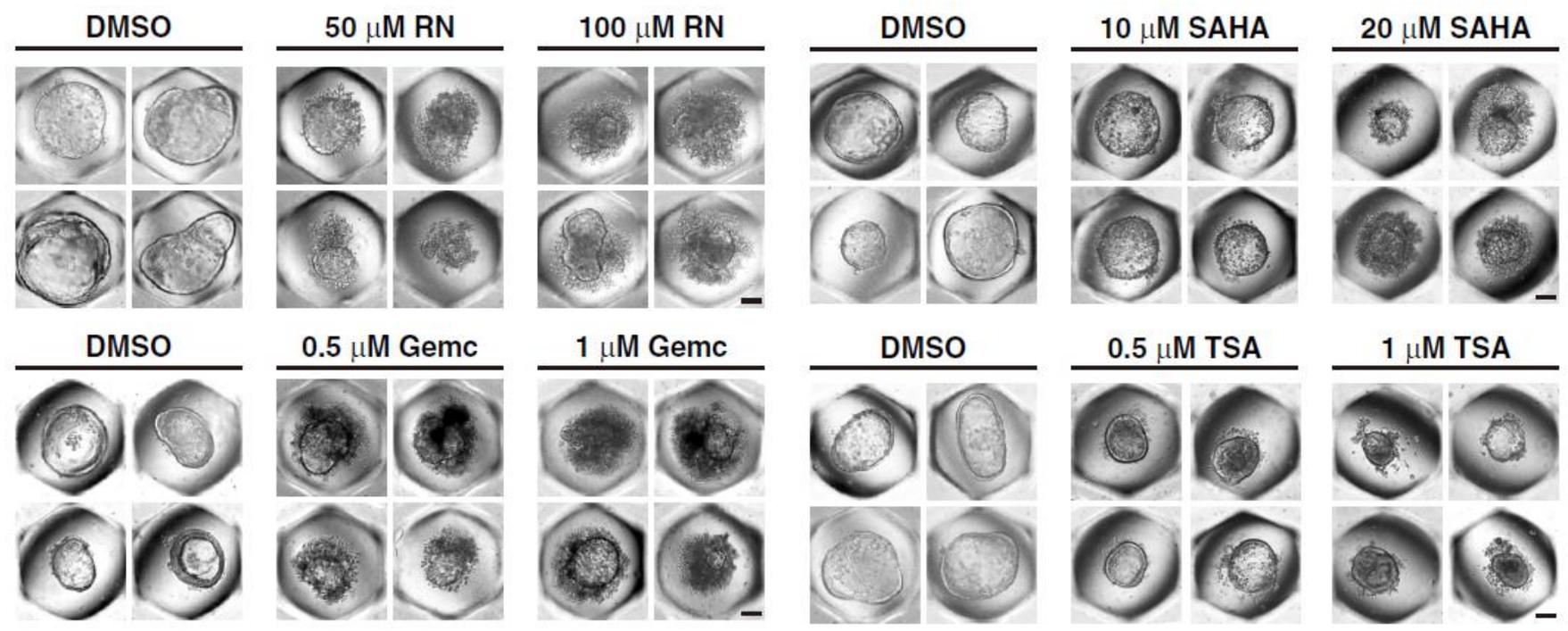
Summary

- We have developed mouse and patient-derived organoids for modeling cancer
- Our microfluidic chip-based oragnoids are efficient mechanism-based drug screening and validation platform
- Multi-omics analysis of organoids reveal novel pathway of pancreas tumorigenesis
- Development of microenvironment on organoids-on-chip may be a promising platform for modeling human cancer and drug screening

CCBG
(Cancer Cell Biology Group)

Current Members

Junyeop Lee
Jennifer Jaeun Lee
Su Hyun Lee
So Young Joo
Sarah Jeon
Jiho Mo
Siyoung Choi
Hong Yul Kim
Hyungmin Kim
Ho Sung Yoo

collaboration

Samsung Medical Center
J. Sophie Park
Sehoon Lee
UNIST
Semin Lee
U. Pennsylvania
DH Bhang
Sandra Ryeom
SNU Chemistry
Seong Keon Kim
SNUH
Young-il Koh
Wonshik Han
Dongyoung Noh
Korea University
Sangjoon Sim
Seok Sid Chung

Former Members

Jiho Park, PhD
Sangjin Paik, PhD
Misun Kwon, PhD
Song Yion Yeu, PhD

Eunhee Choi, PhD
Jaewon Min, PhD
Pil-Gu Park, PhD
Hae-Ock Lee, PhD

Yookyung Lee, MD PhD
Inai Park, PhD
KW Hyung, PhD
HY Jeon, phD