

# Basic Pancreatic Cancer research collaborate with surgeons and researchers



University of Tsukuba, Dept. GI & HBP Surgery  
Osamu Shimomura

# COI Disclosure

下村 治

Osamu Shimomura

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講演内容に関連し、演者について開示すべきCOI関係にある企業等はありません。

The speaker have no financial conflicts of interest to disclose concerning the presentation.

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- About Pancreatic cancer
- Glycan analysis of pancreatic cancer
- Glycan targeting cancer therapy with “lectins”

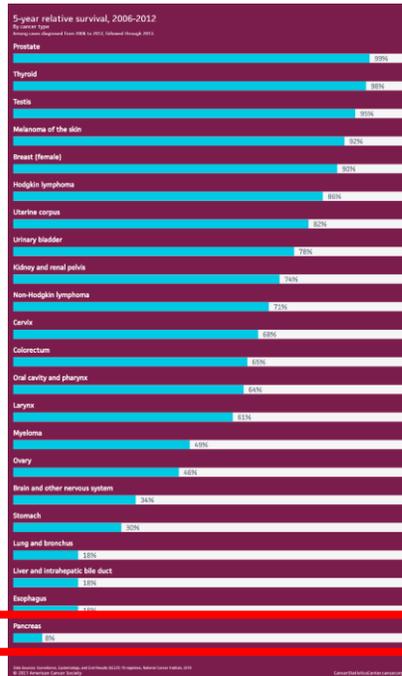


# Pancreatic cancer is the lethal disease

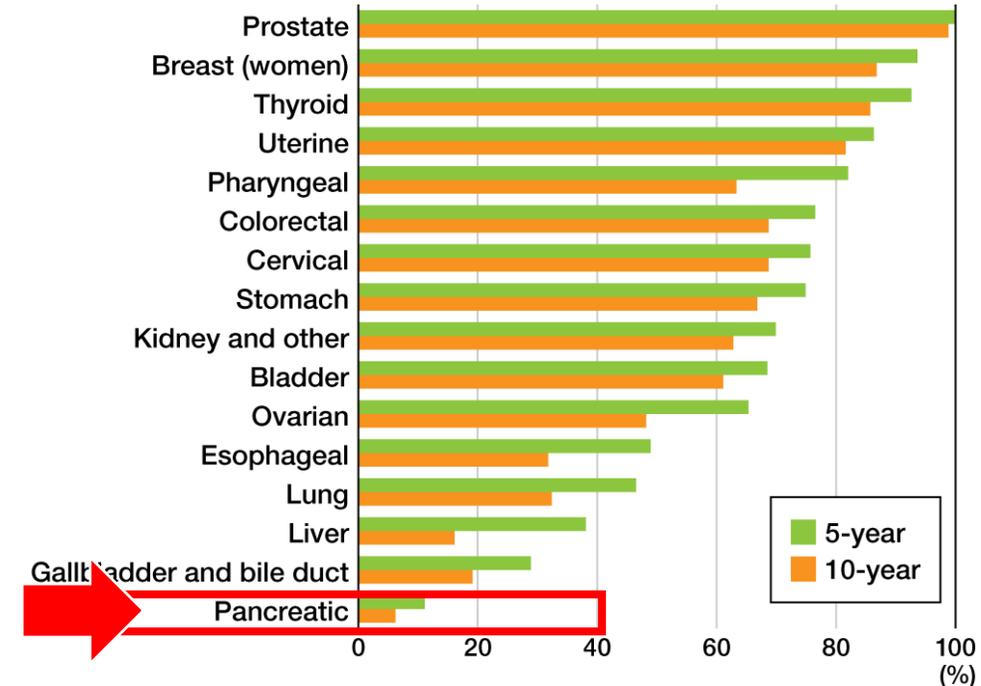
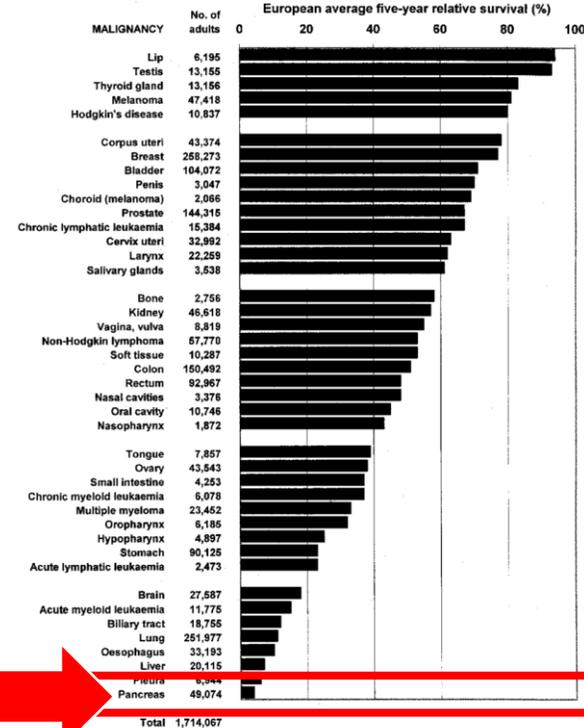
About 5y survival  
Japan

U.S.

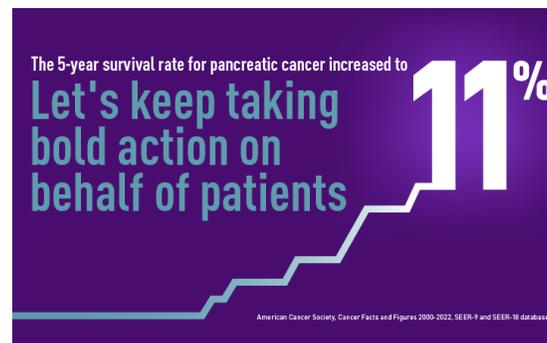
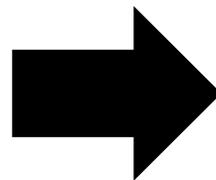
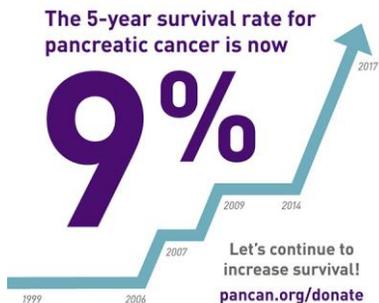
Europe



From American Cancer Society



From National Cancer Center



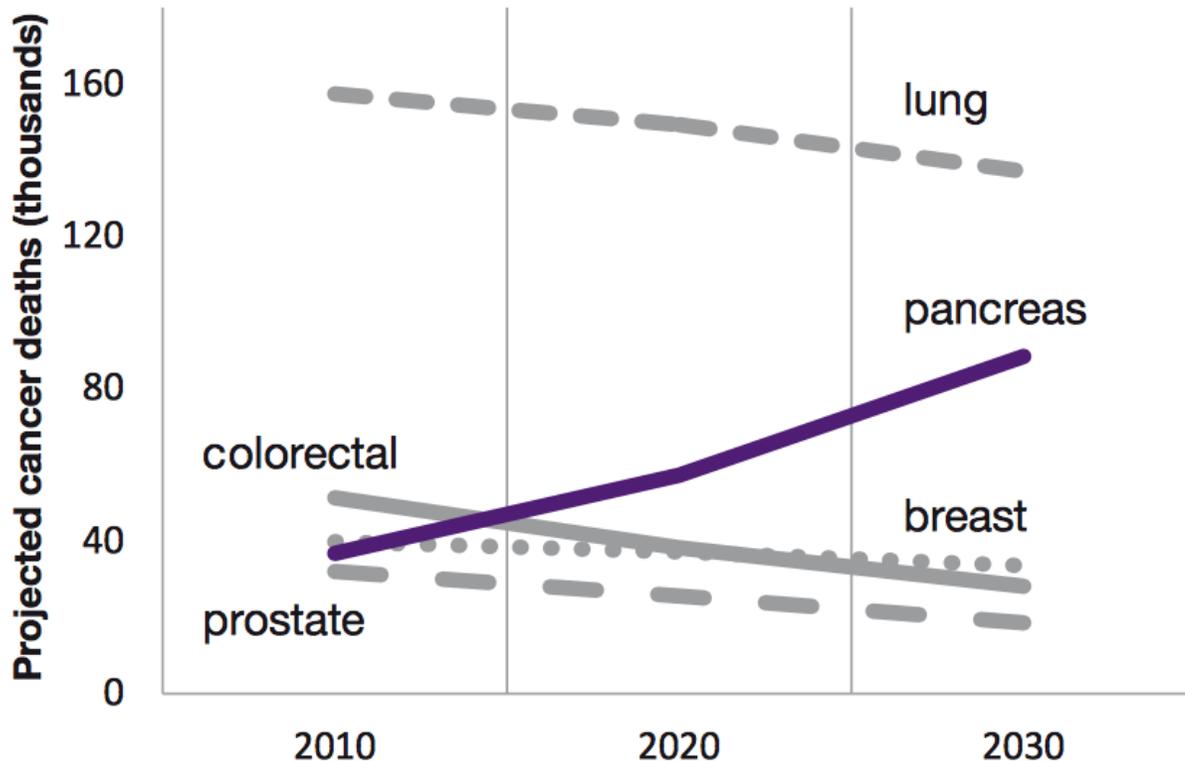
Up to 10% in 2 decades



# Pancreatic cancer patients are increasing

## Forecast of the U.S.

### PROJECTED CANCER DEATHS



2014 AACR News Releases, Lynn Matrisianより

## Japanese real data

Number of death from pan. cancer

2014 Male: 5<sup>th</sup> 16,411  
Female: 4<sup>th</sup> 15,395  
Total = 31,800



2018 Male: 4<sup>th</sup> 18,124  
Female: 3<sup>th</sup> 18,232  
Total = 36,300

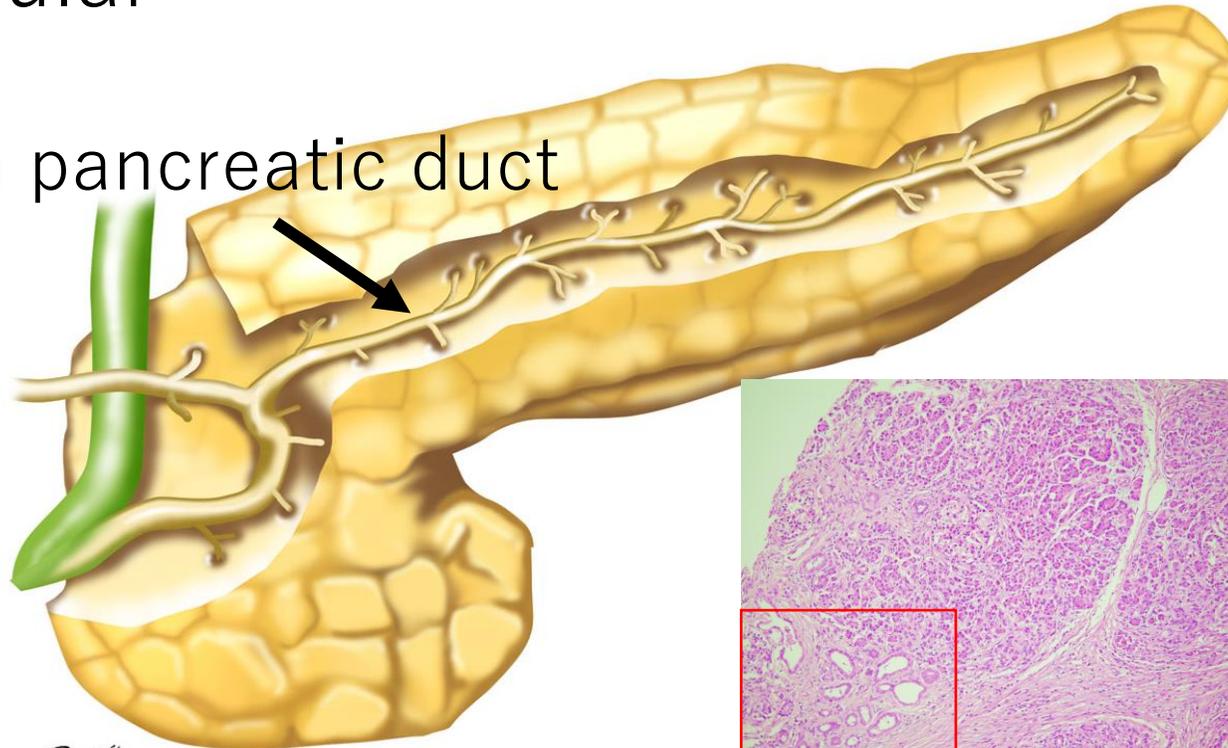


# Derive of pancreatic cancer

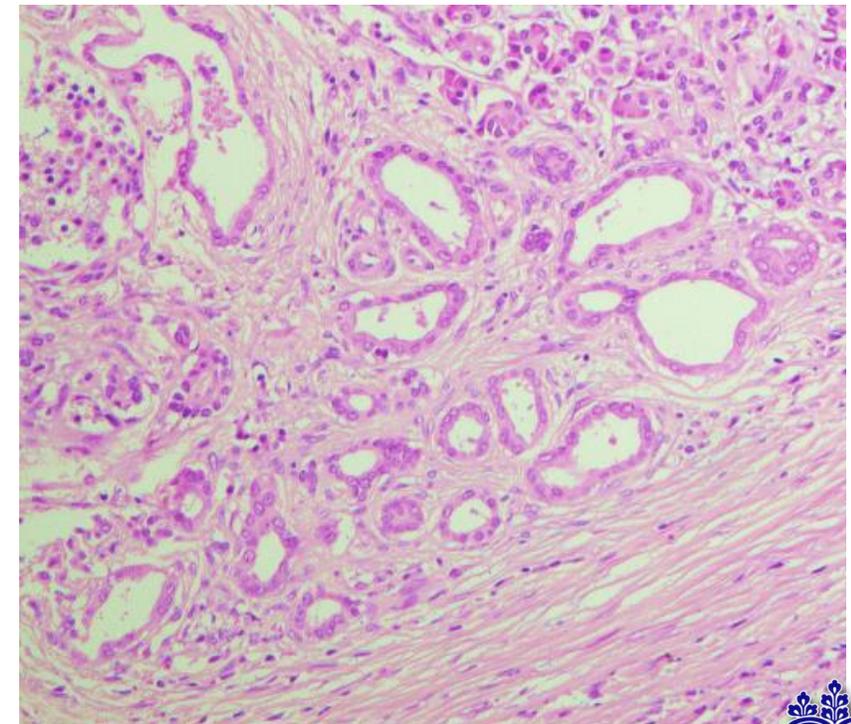
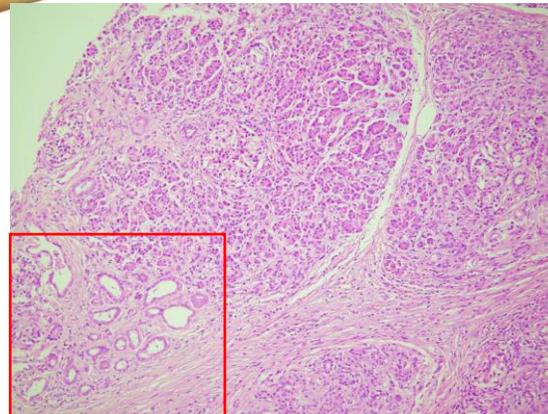
Pancreatic duct is the origin of cancer

「**Invasive ductal adenocarcinoma**」 is the most popular

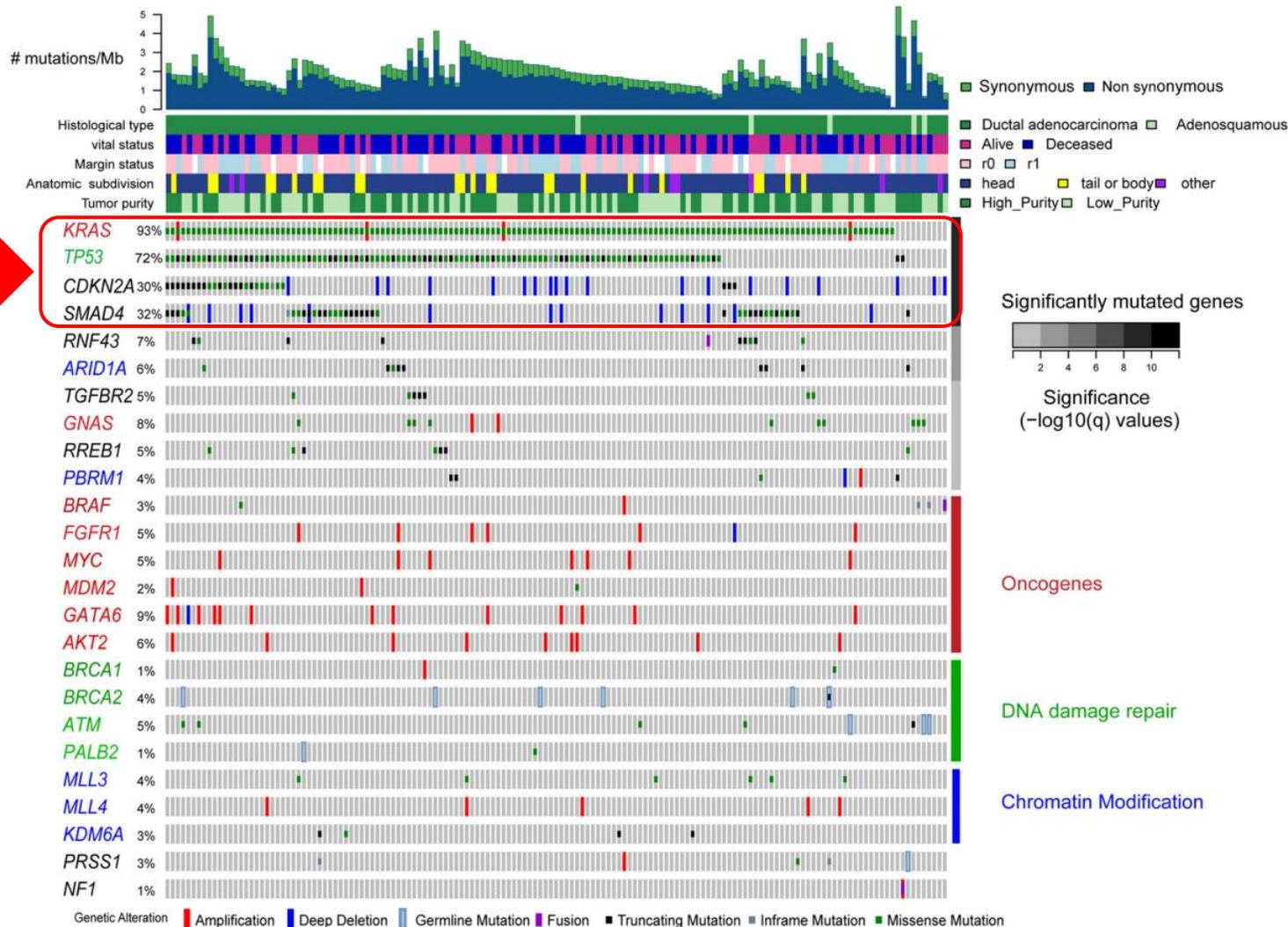
Main pancreatic duct



*S. Saito*  
2011 ©



# Genomic characterization of Pancreatic cancer

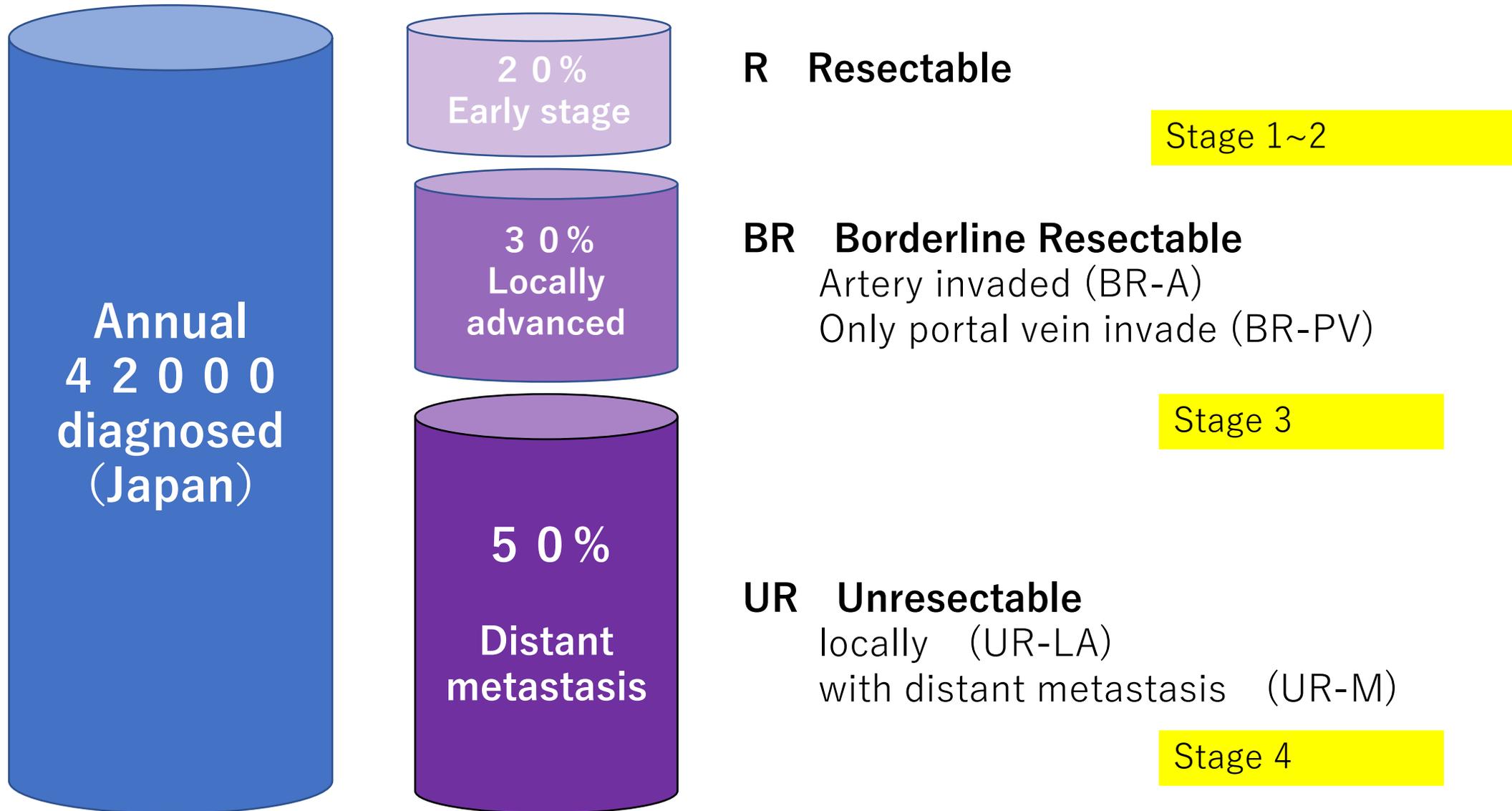


Related big 4 genes

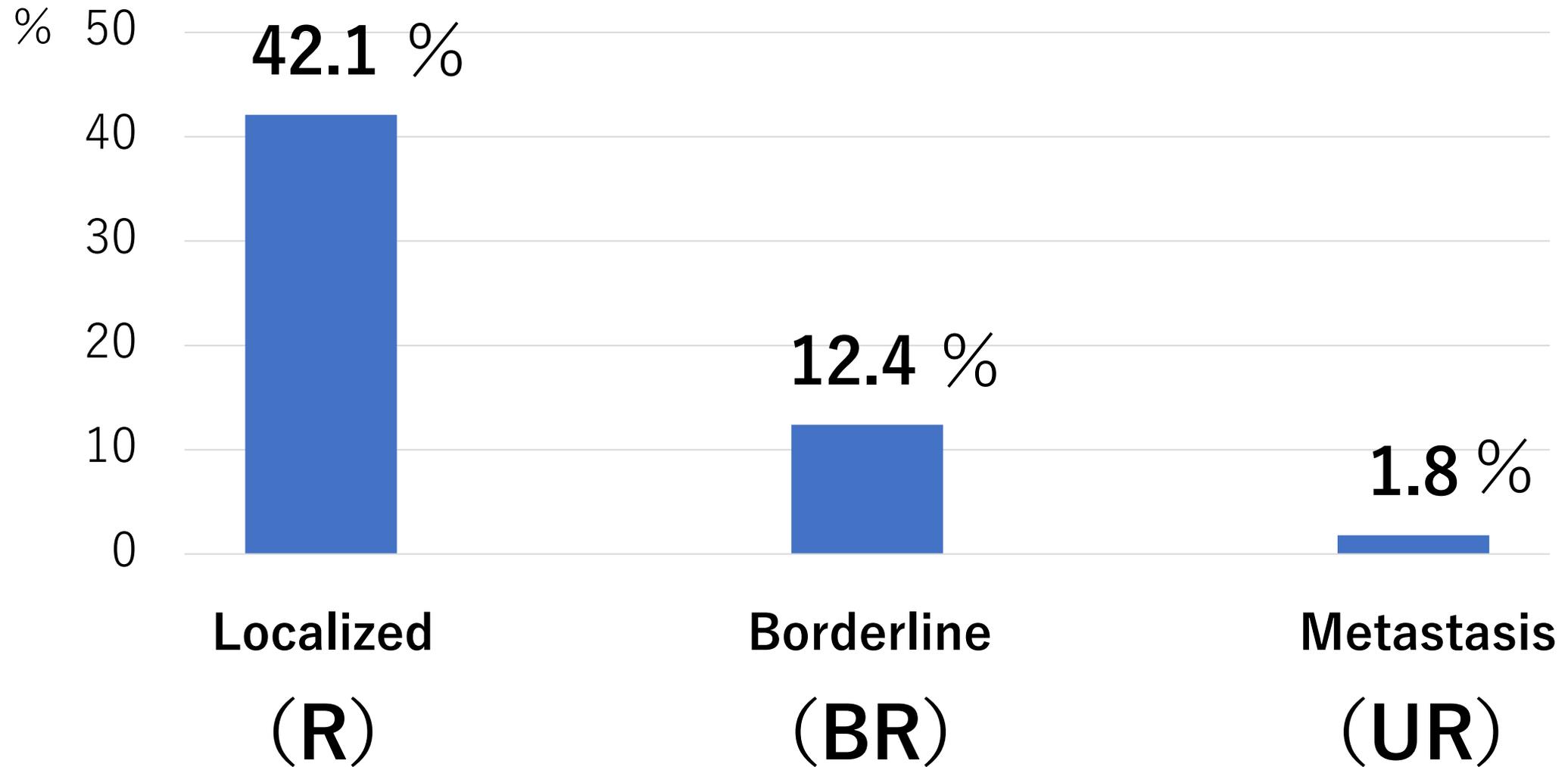
KRAS 93%  
 TP53 72%  
 CDKN2A 30%  
 SMAD4 32%



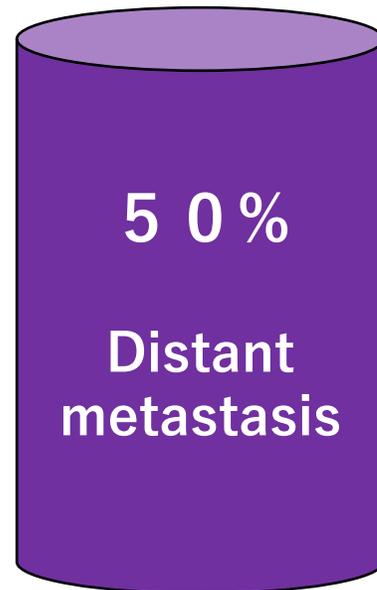
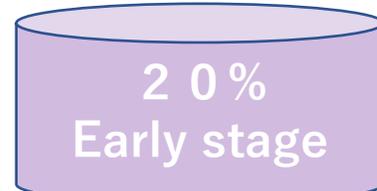
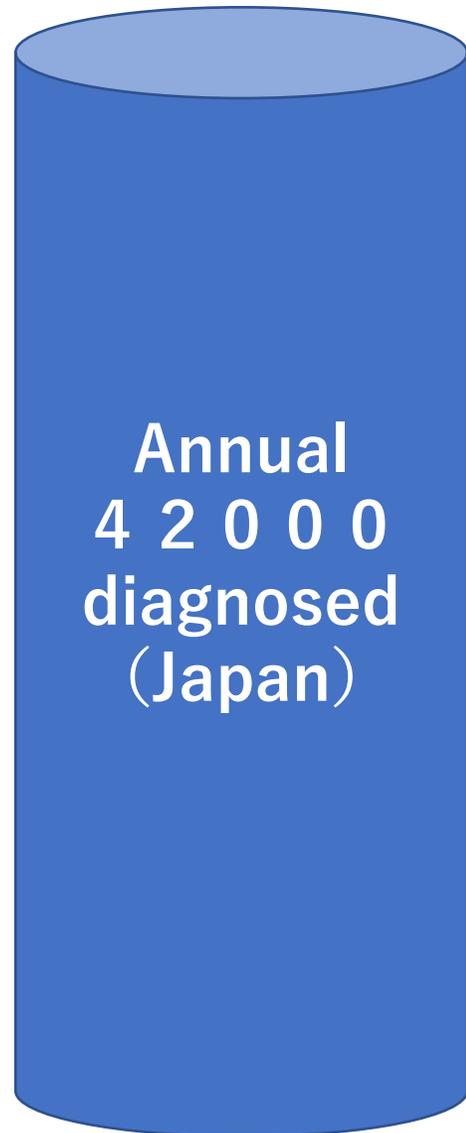
# Only 20 % are candidates of cure resection



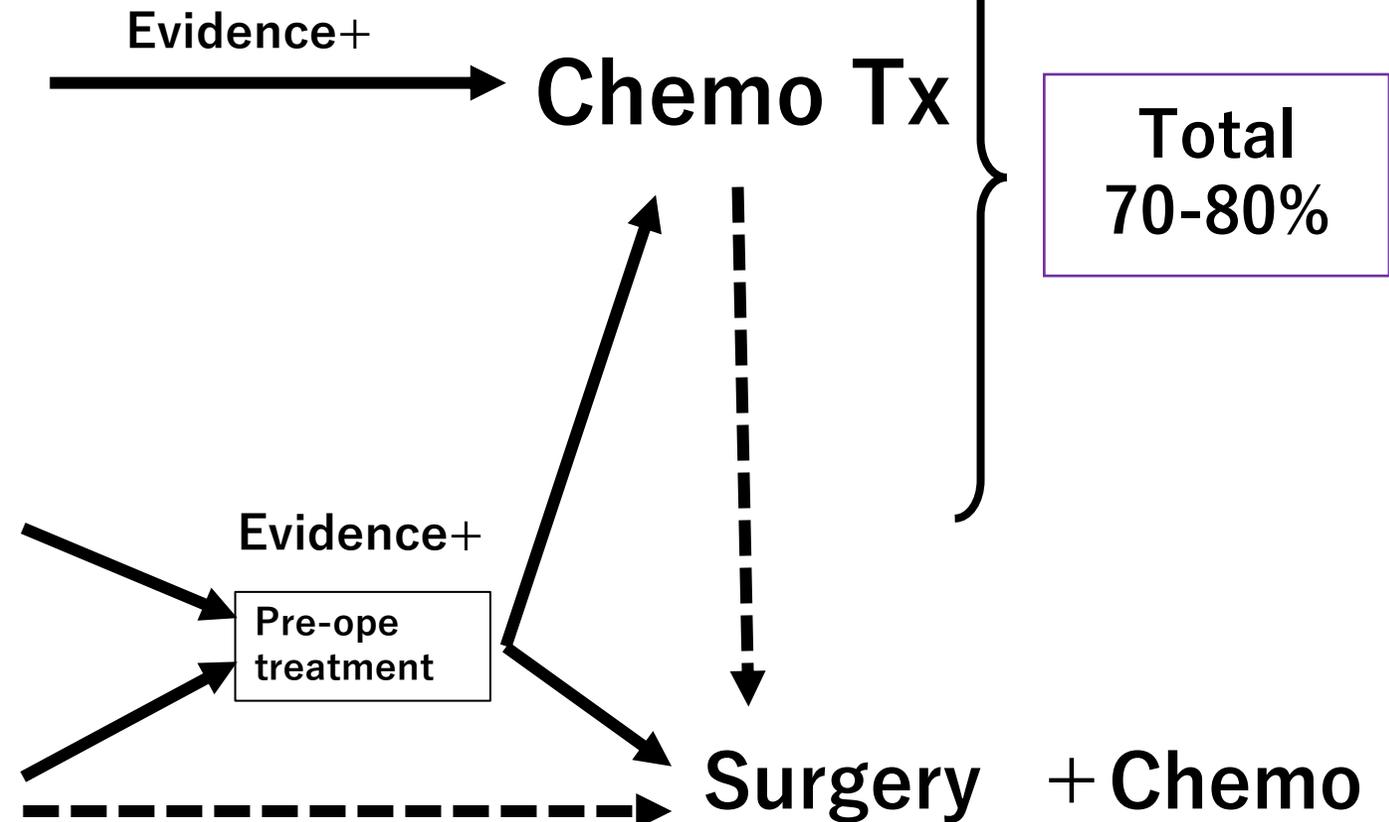
# 5y survival rate at each stage



# Treatment strategy



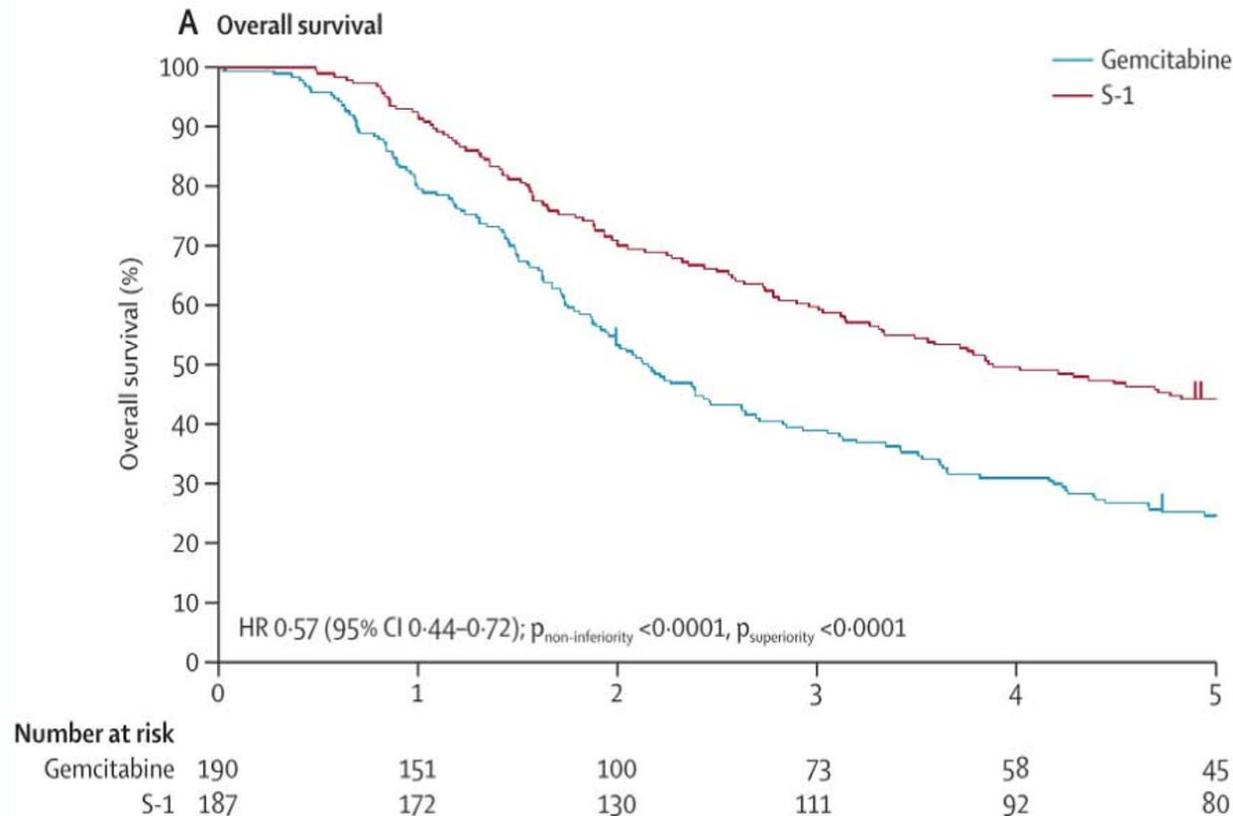
All patients require  
chemotherapy



# Surgery with chemotherapy for resectable patients

20%  
Early stage

Uesaka K et al., Lancet 2016

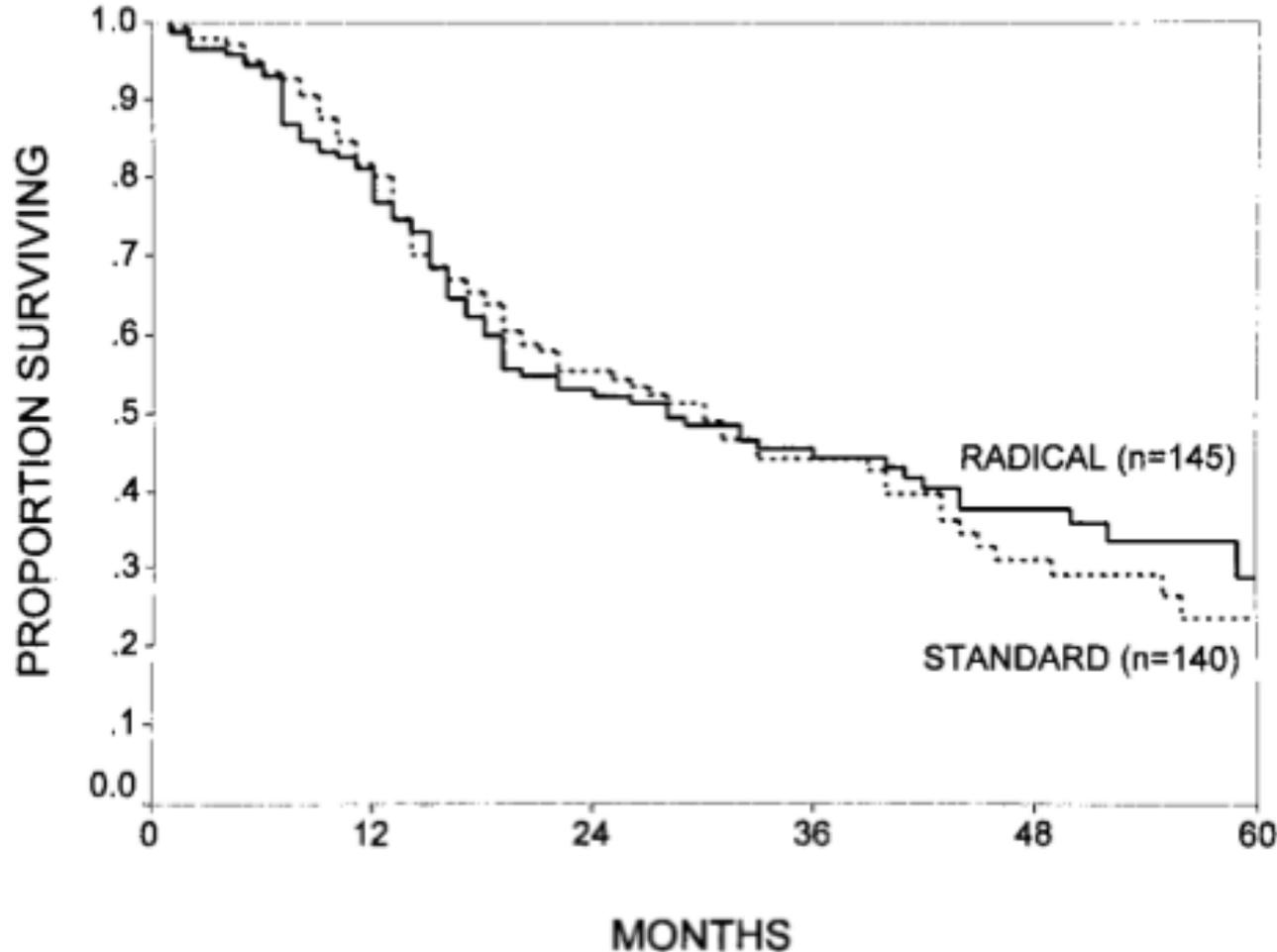


5y survival: 44.1%  
5y disease free survival:  
33.3%



# The effect of Extended vs Standard surgery

(2002 The Johns Hopkins Medical Institutions, Baltimore, USA)



Extended vs. Standard lymphadenectomy

**No difference**

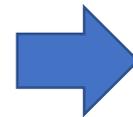
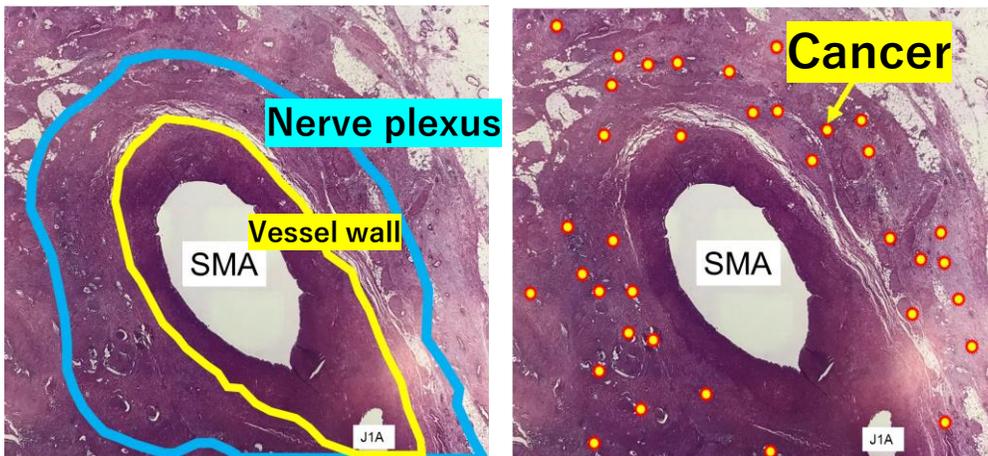


# Extended lymphadenectomy did not extend survival

	Italy	USA J Hopkins	USA Mayo	Japan	Korea
publish	1998	2002	2005	2012	2014
Pt number	40 vs 41	146 vs 148	40 vs 39	51 vs 50	83 vs 86
Survival <b>standard vs Ex</b> Month(median)	11.2 vs 16.7	30 vs 28	26 vs 18.8	19.9 vs 13.8	18.8 vs 16.5
Prognosis	<b>N.S.</b>	<b>N.S.</b>	<b>N.S.</b>	<b>N.S.</b>	<b>N.S.</b>

From General Rules for the Study of Pancreatic Cancer 7<sup>th</sup> Edition

(Tsutomu Fujii, Kawai Manabu et al., The bible of Pancreatic cancer treatment (in Japanese) p 174)

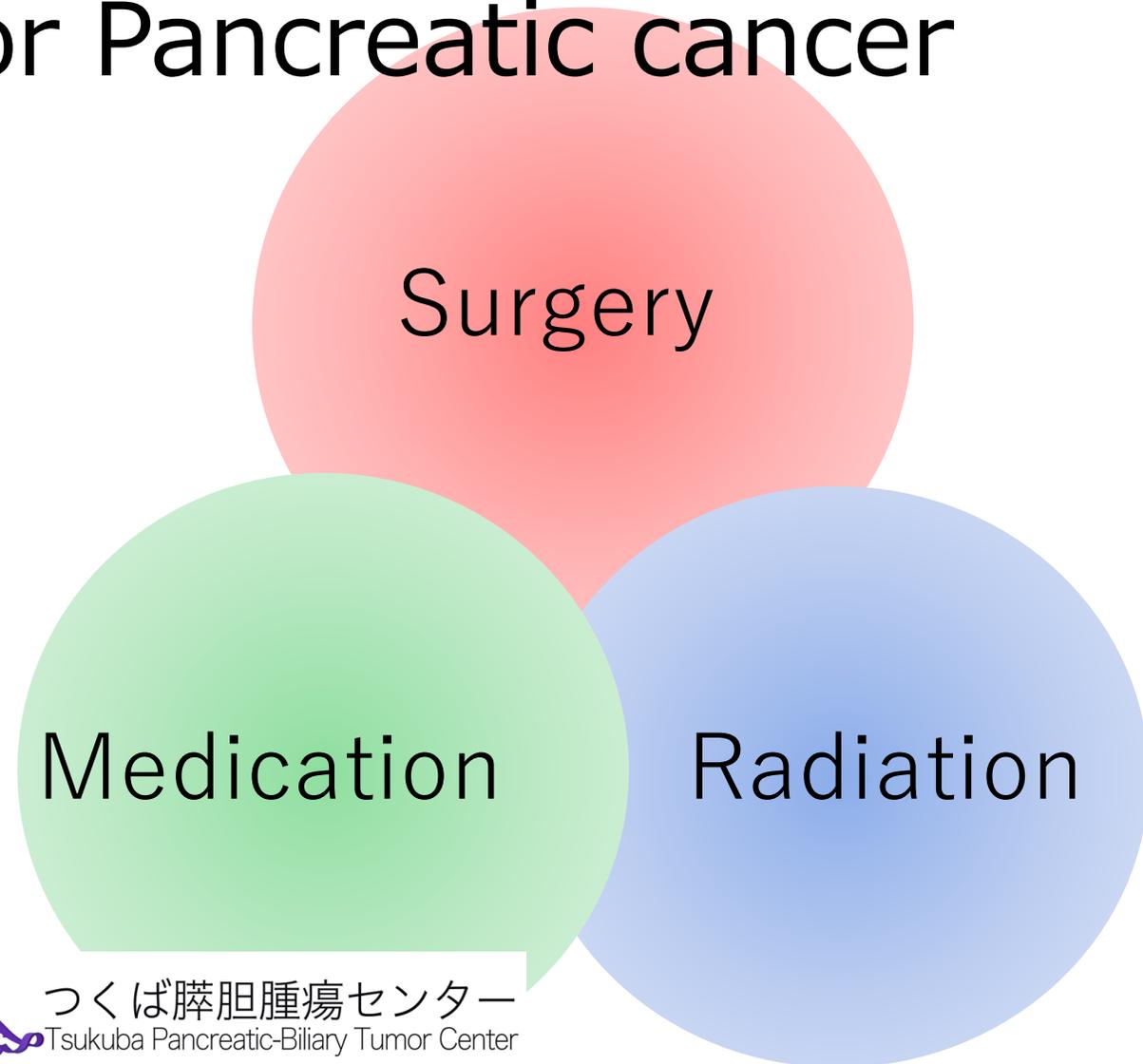


**Surgery itself may be difficult to prolong patient survival**

SMA: Supra Mesenteric Artery



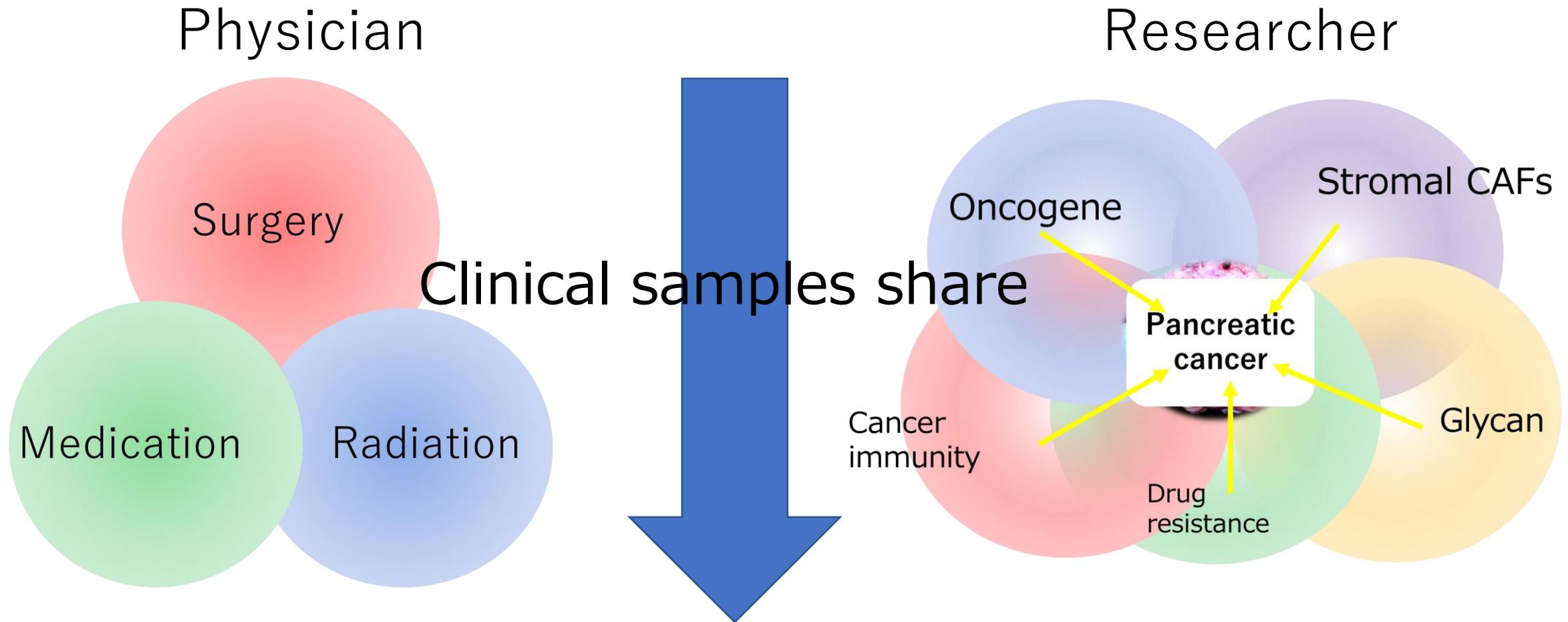
# Treatment with multi-modality strategy for Pancreatic cancer



**Surgery**  
+  
**Chemotherapy**  
+  
**Radiation**  
  
**= For cure**



# Challenge for pancreatic cancer



Collaboration is important



# To improve pancreatic cancer patient survival

- 1、 Early detection、 improve the resection rate
- 2、 Develop the innovative anti-cancer drugs
- 3、 Introduce true personalized medicine based on disease status

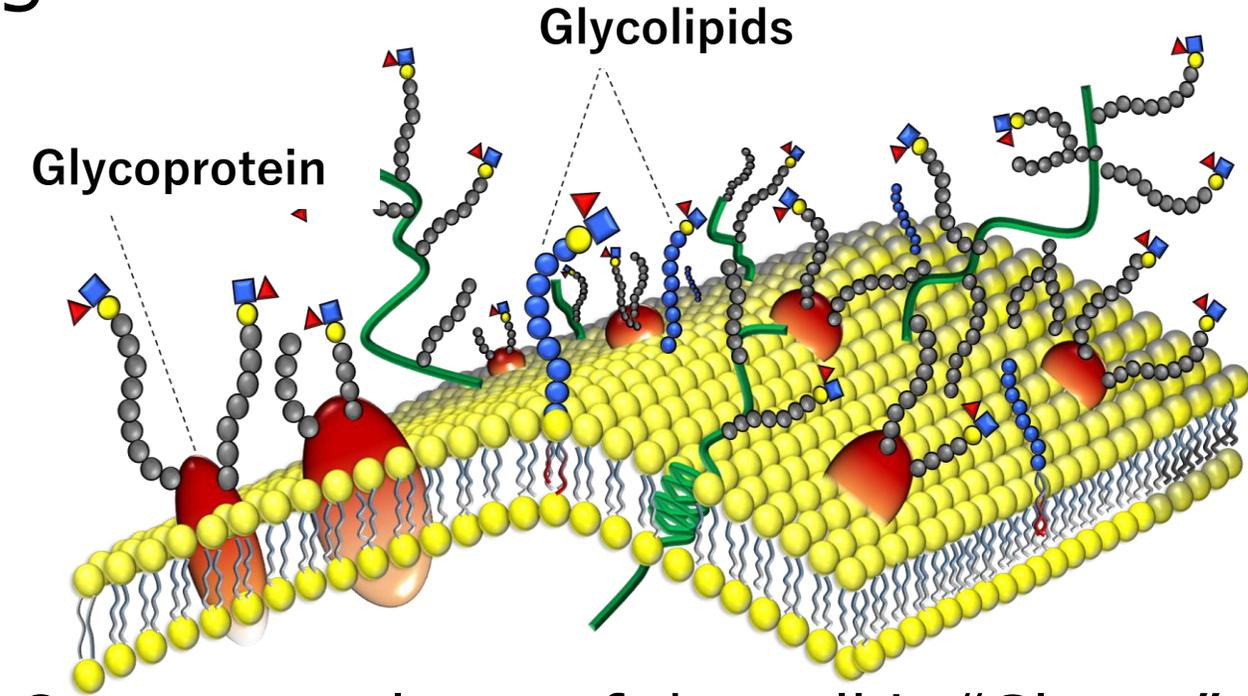
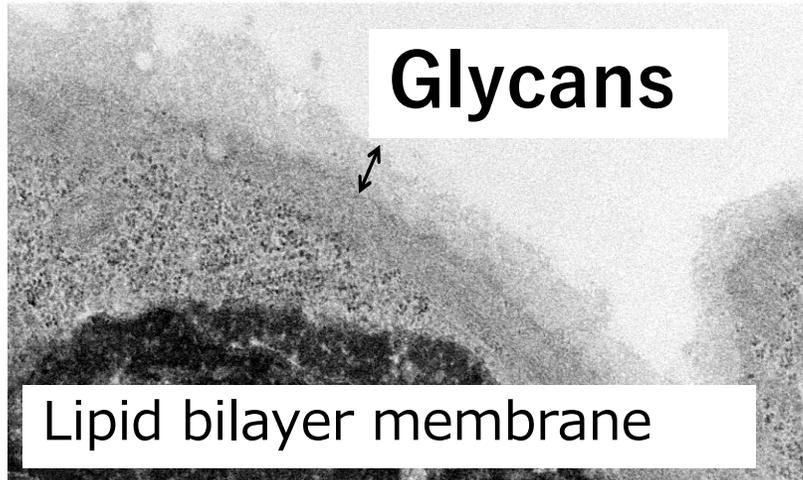


# Contents

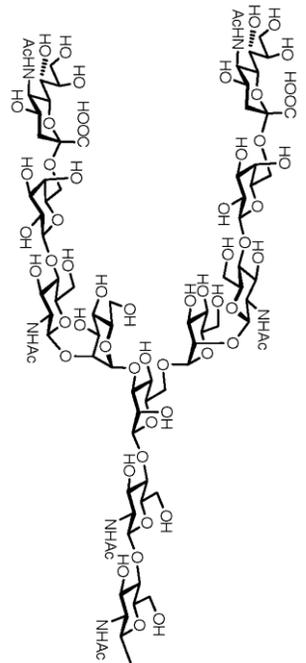
- About Pancreatic cancer
- Glycan analysis of pancreatic cancer
- Glycan targeting cancer therapy with “lectins”



# Cell specific "Glycans" are attractive as cancer diagnosis and therapeutic targets



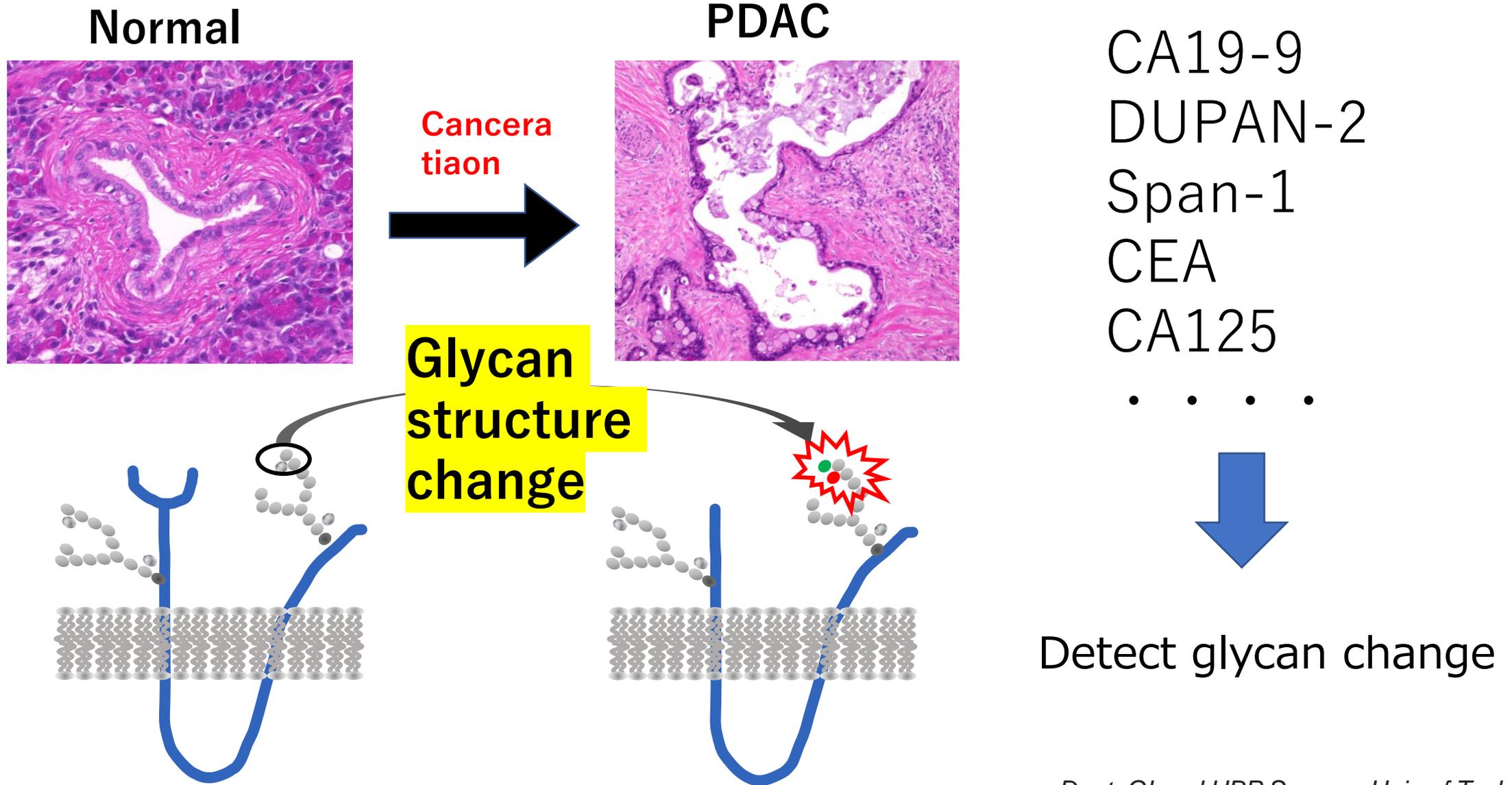
Outer most layer of the cell is "Glycan"



Diagnosis and treatment development focusing on glycosylation



# Tumor biomarkers detect glycan changes

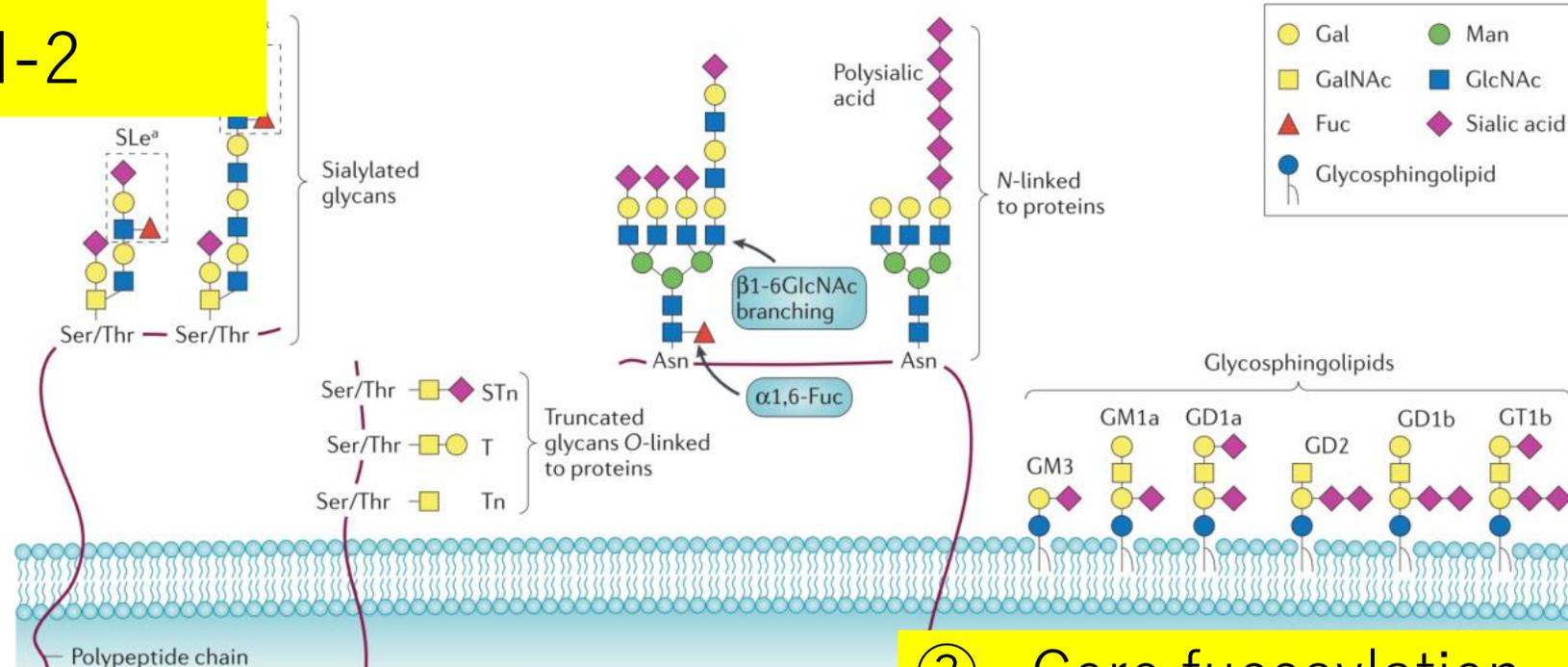


# Glycan changes in cancer progression

Pinho, S. S. and C. A. Reis (2015). Nat Rev Cancer 15(9): 540-555.

① Sialylation  
CA19-9  
DUPAN-2

④ Branched *N*-glycans

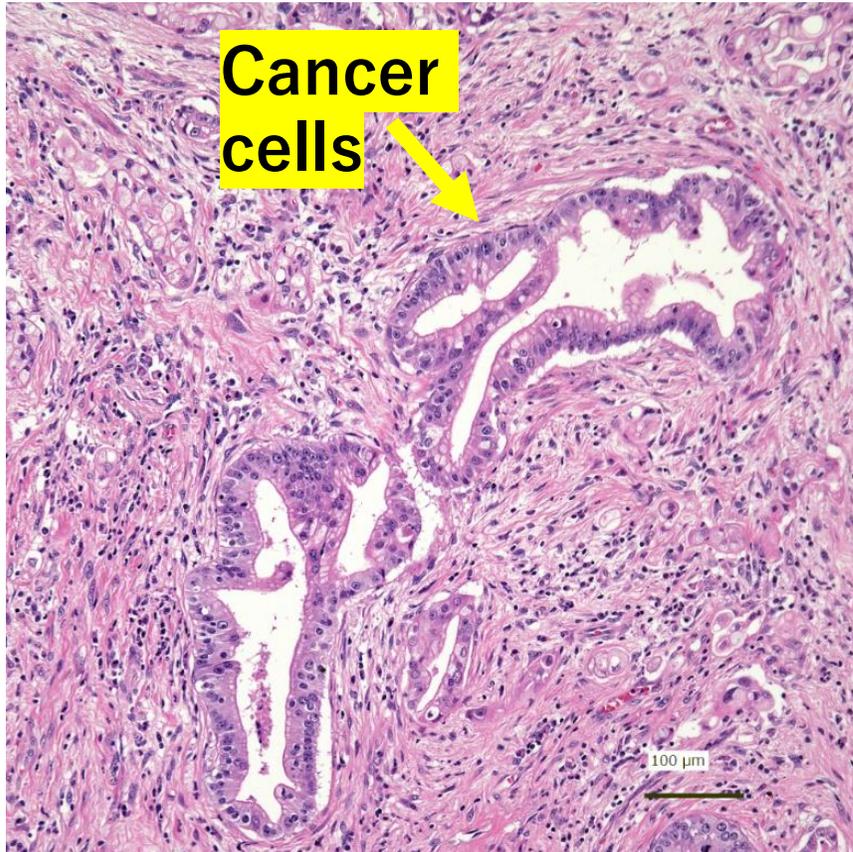


② Truncated *o*-glycan

③ Core fucosylation  
AFP-L3 = core fucosylation of AFP



# Challenges for glycan analysis of pancreatic cancer



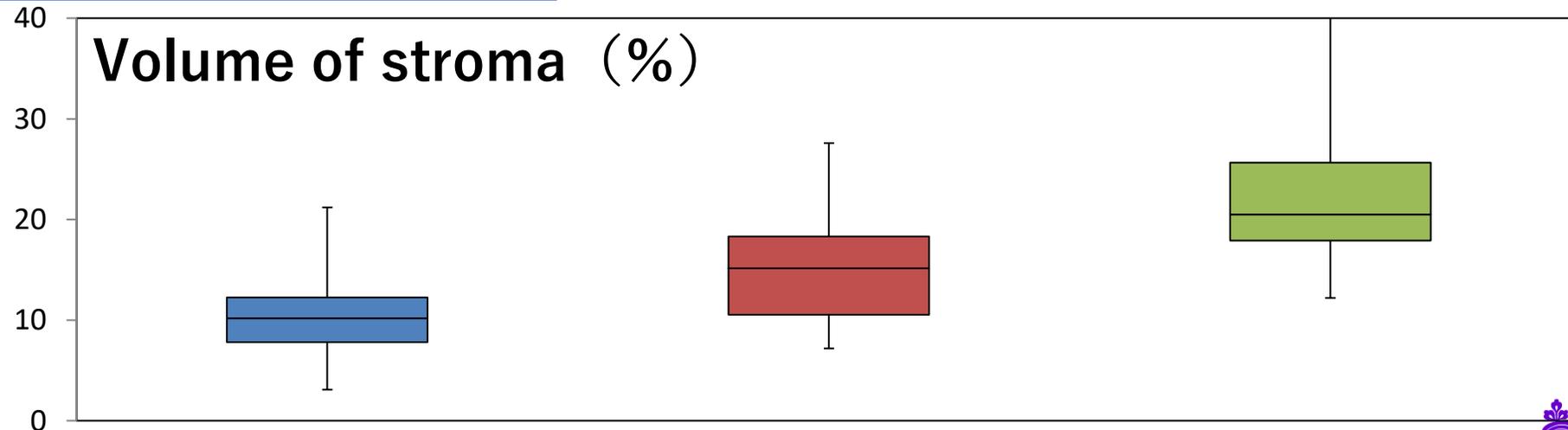
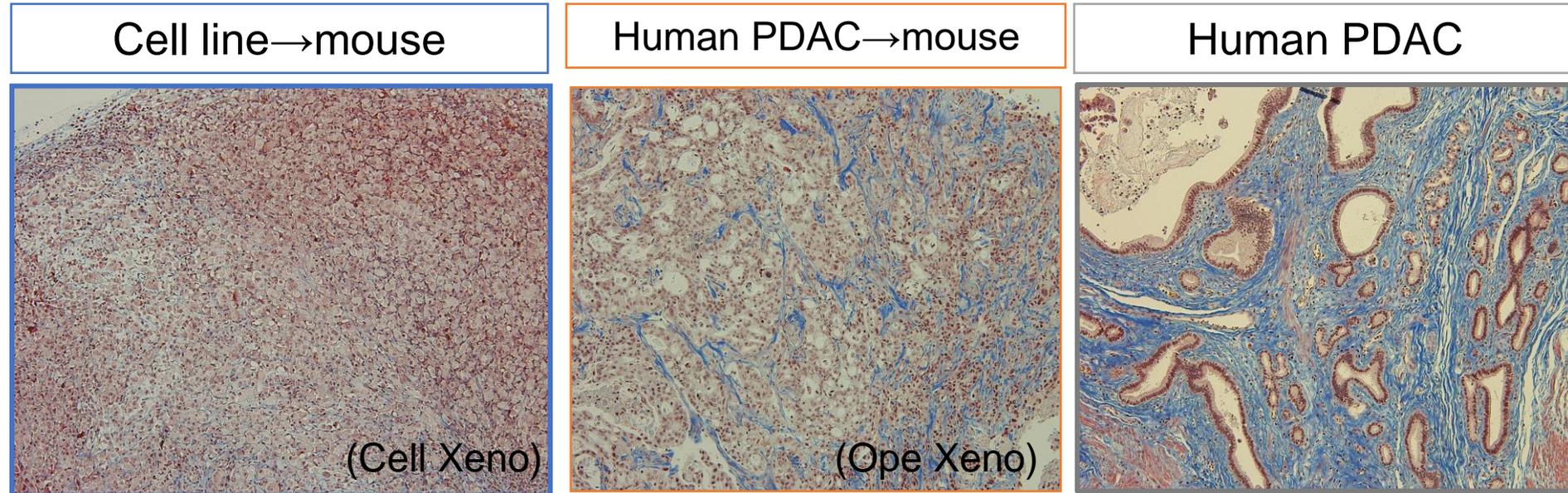
Pathology of PDAC

- ✓ Tumor Heterogeneity
- ✓ Abundant stroma



# Stromal cells between pancreatic cancer models

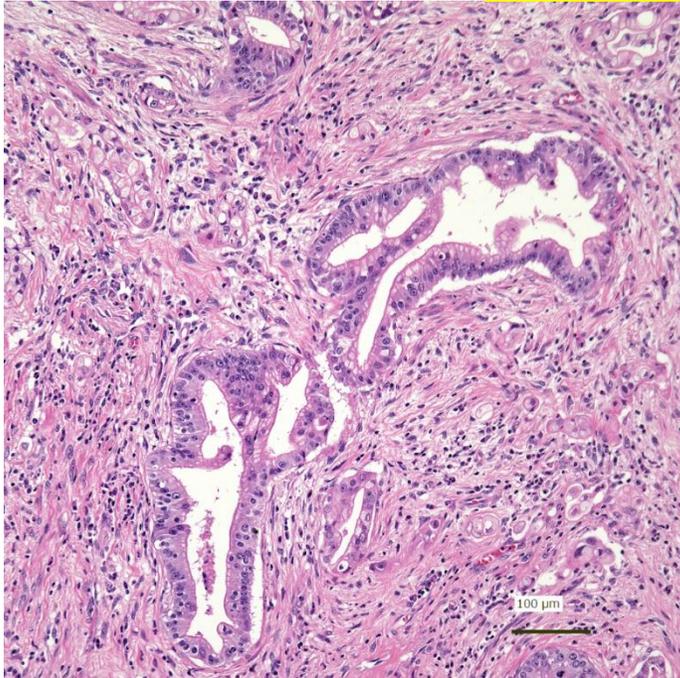
Akashi Y, Oda T et al., Pancreas 2013



# "Capan-1" represents clinical PDAC morphology

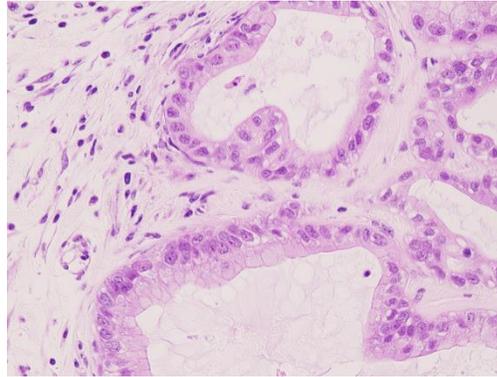
Clinical PDAC

**g++/s++**

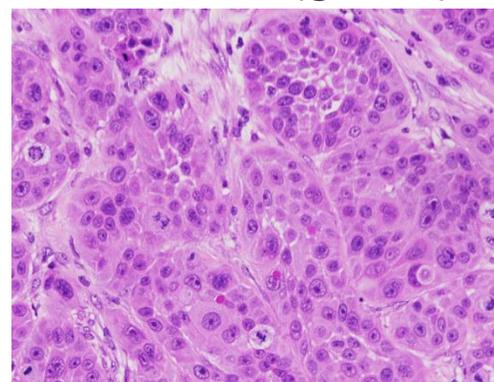


Cell xenograft

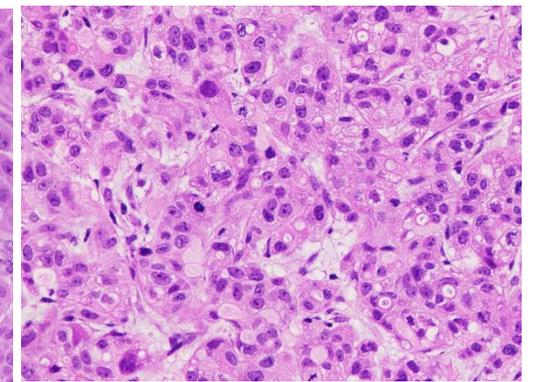
Capan-1 (**g++/s++**)



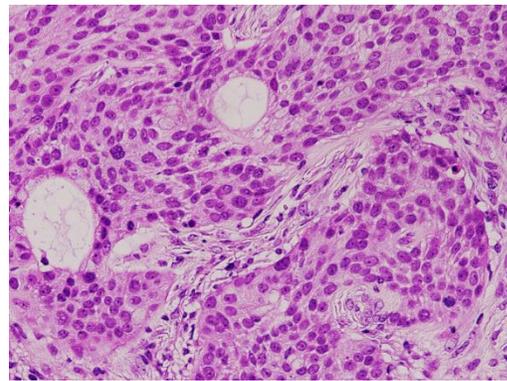
BxPC-3 (g+/s+)



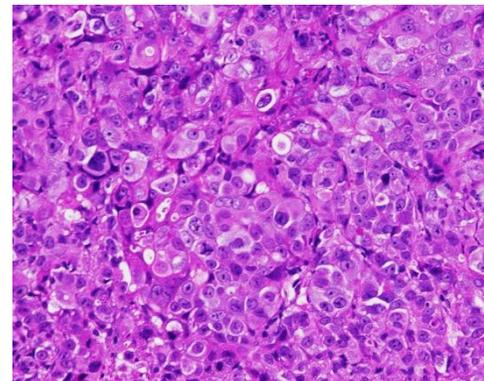
ASPC-1 (g+/s-)



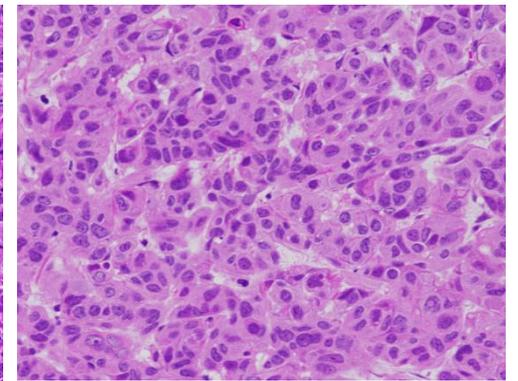
MIAPaCa-2 (g-/s+)



PANC-1 (g-/s-)



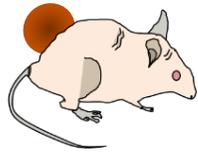
SUIT-2 (g-/s-)



**Ductal spread (g -/+ /+++),  
Stromal volume (s -/+ /+++)**

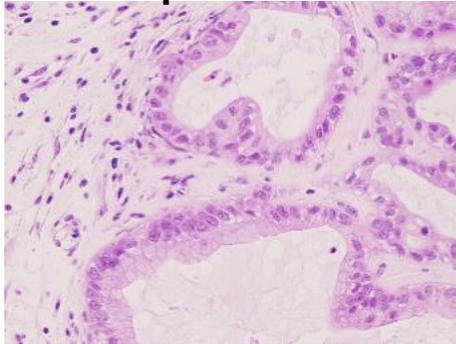


# Glycan analysis of PDAC cell lines by lectin microarray



Xenograft morphology

Capan-1



PDAC  
Cell lines

VS

Pancreatic cancer cell lines

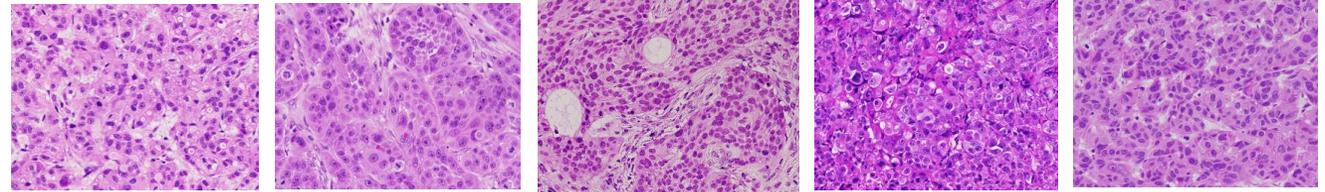
ASPC-1

BxPC-3

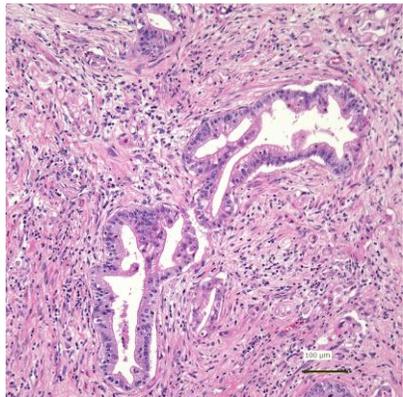
MIAPaCa-2

PANC-1

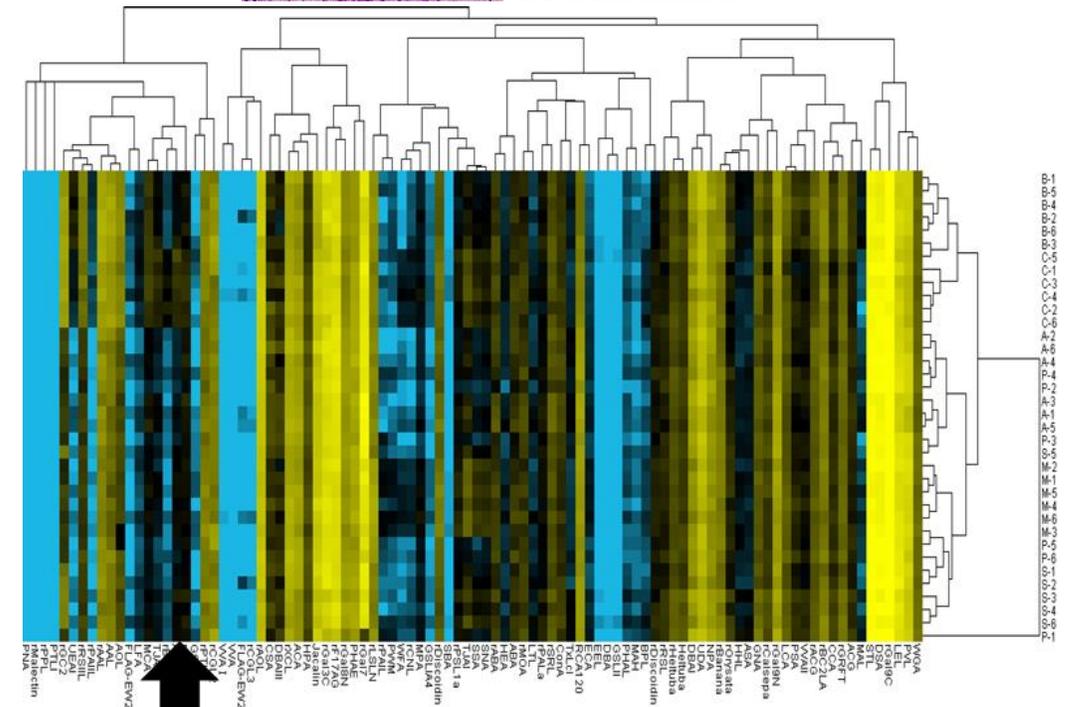
SUIT-2



Clinical sample



Lectin microarray



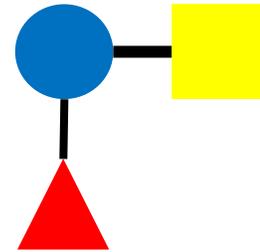
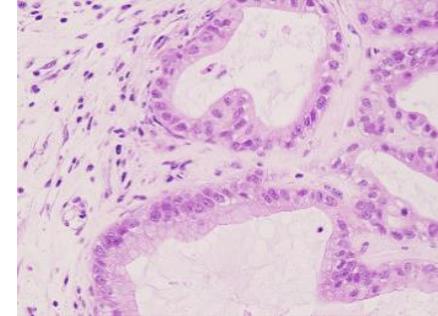
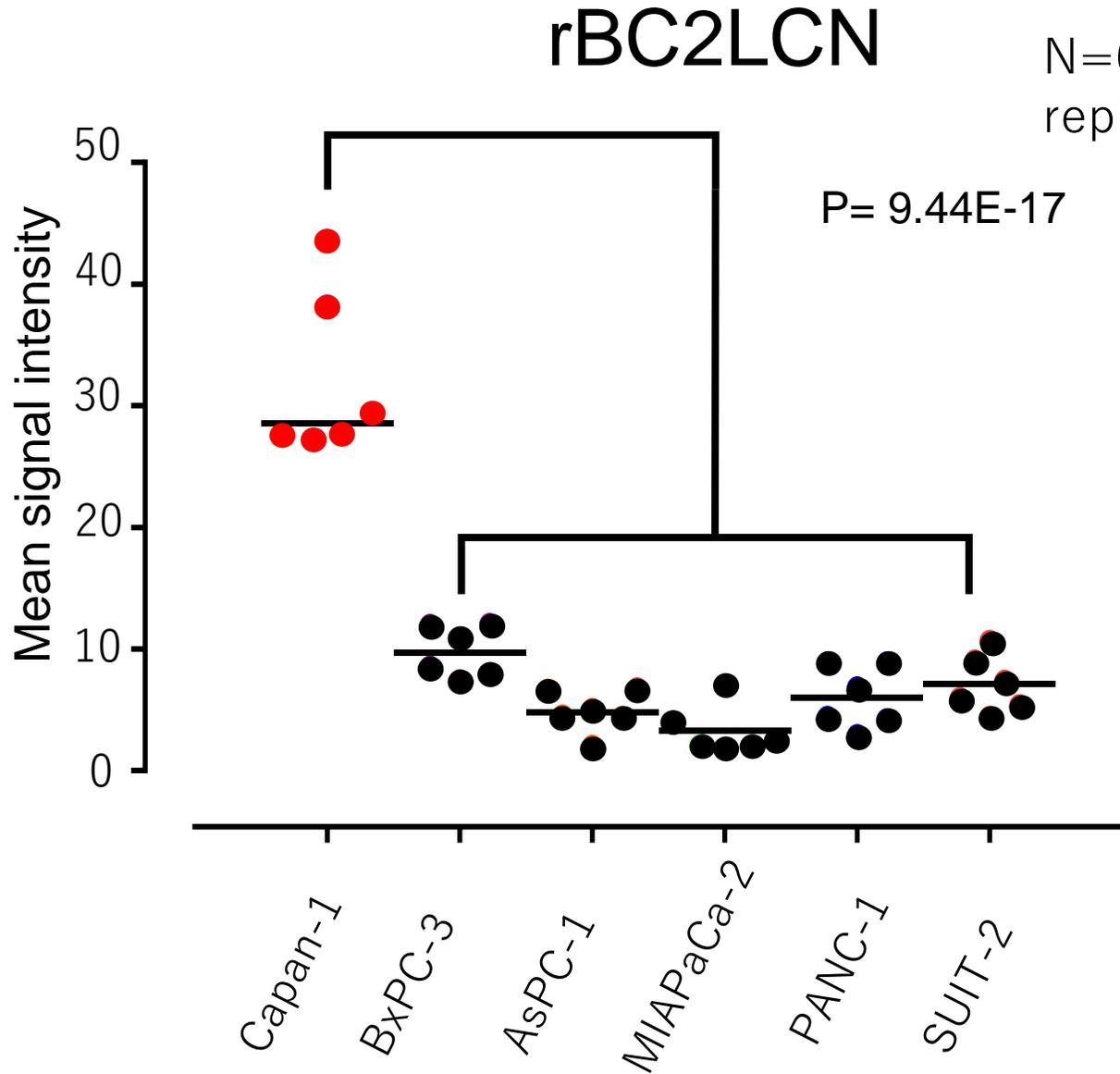
rBC2LCN lectin



96 lectins



# rBC2LC-N recognize the Capan-1 cell lines



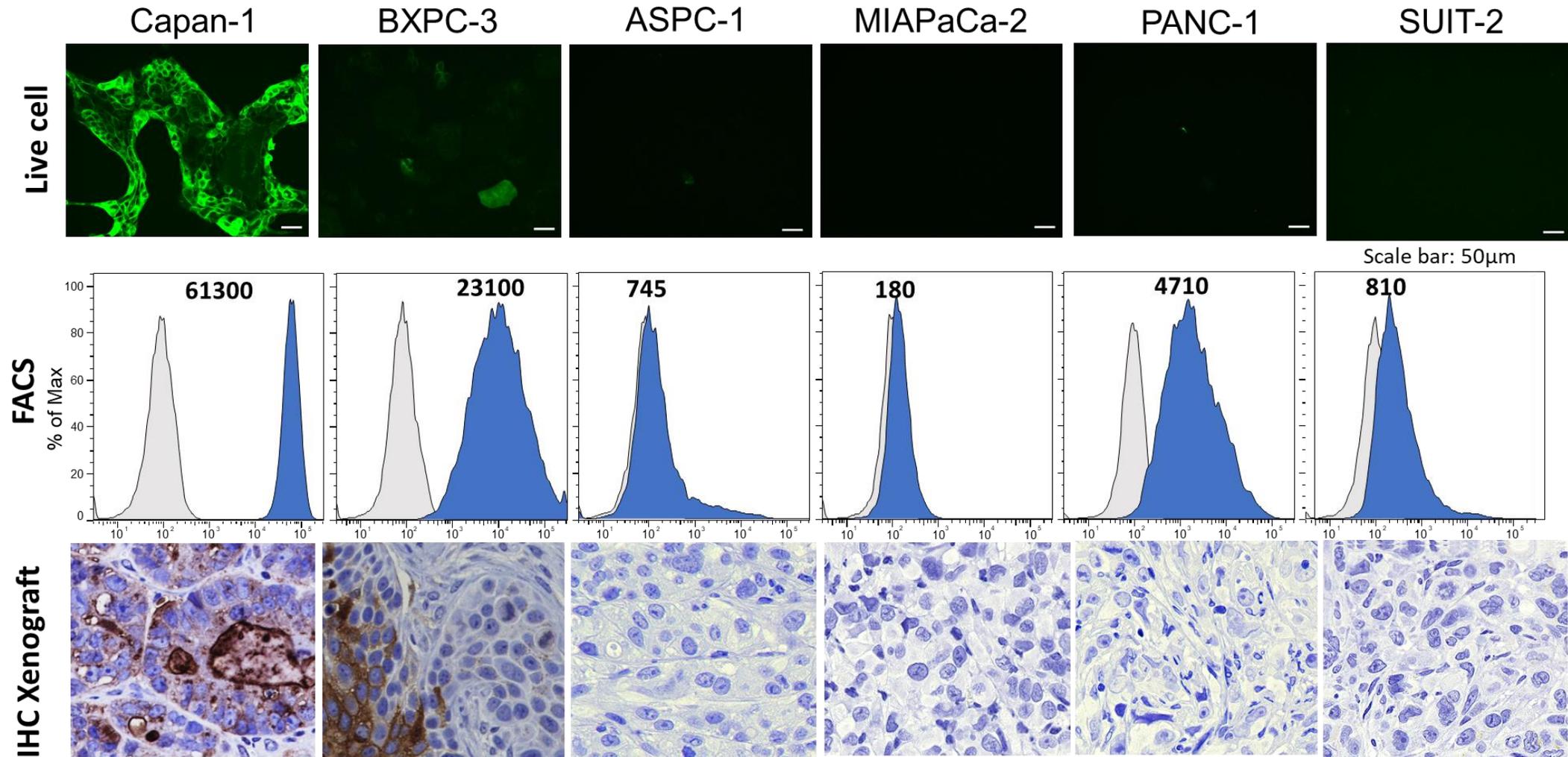
## H type 1/3/4 structure

Fuc  $\alpha$  1-2Gal  $\beta$  1-3(GlcNAc or GalNAc or Glc)  
H type 1, Lewis b and Lewis Y sequences

Sulak, O., et al. *Structure* 2010



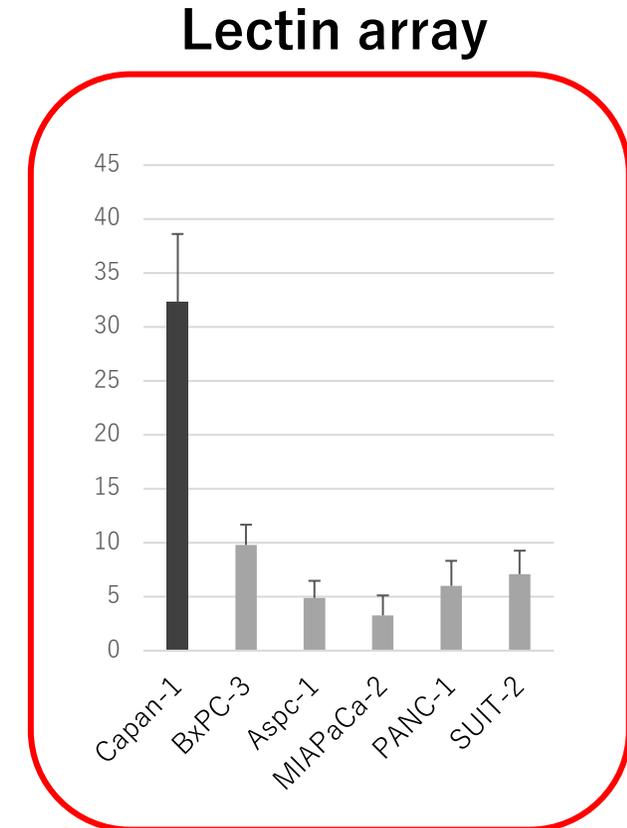
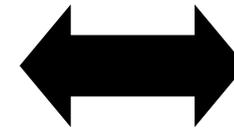
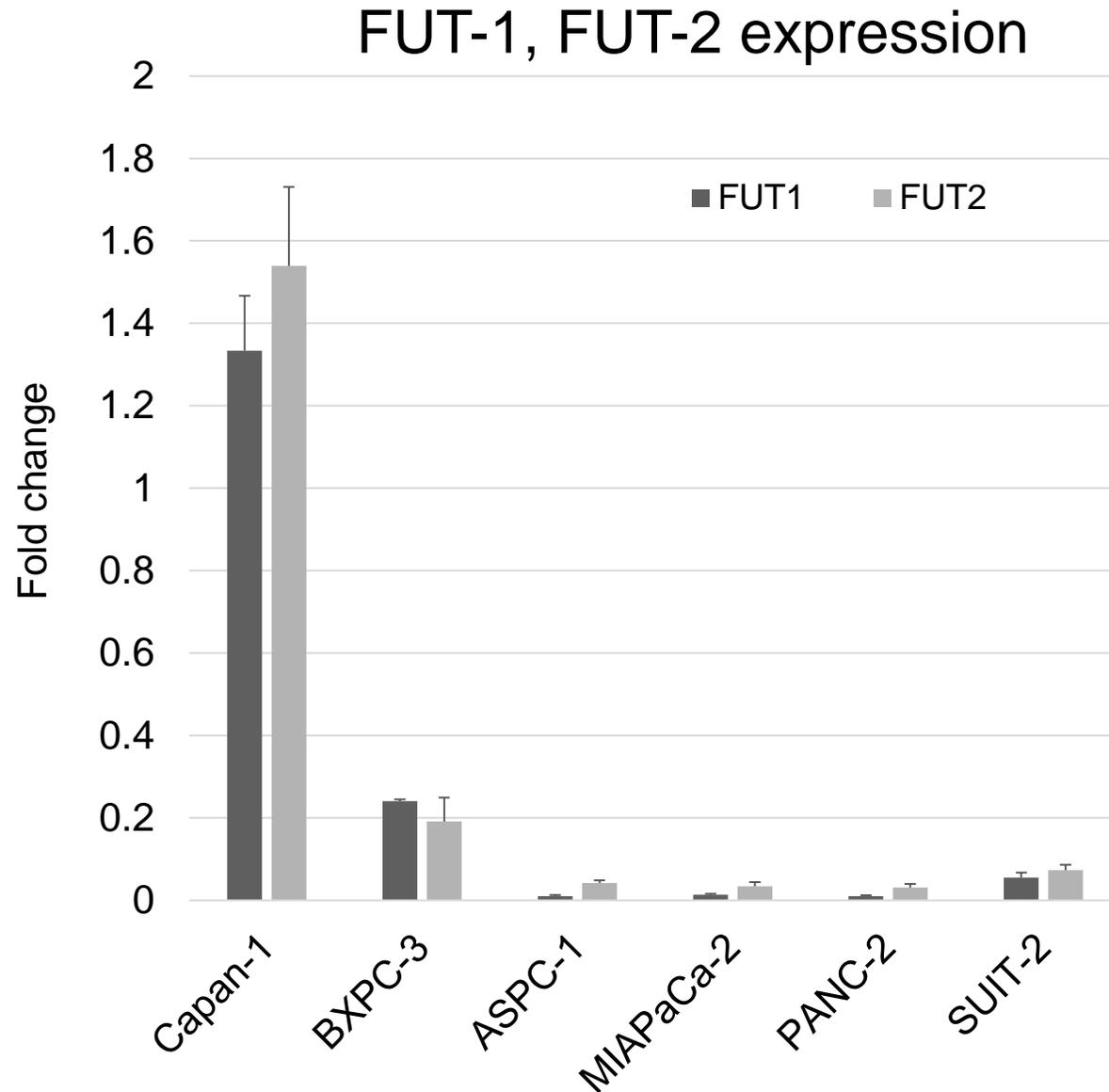
# rBC2LCN reactivity to other PDAC cell lines



マウス皮下腫瘍の染色



# FUT1, FUT2 gene expression in cell lines

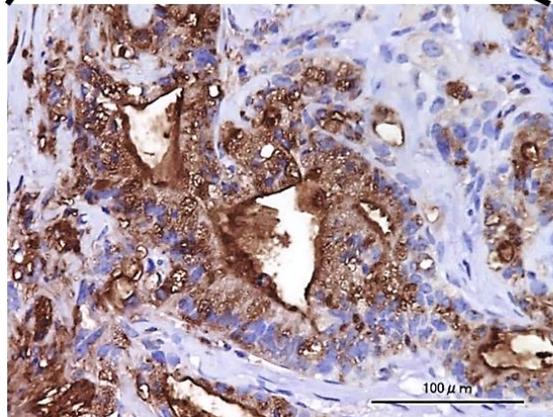
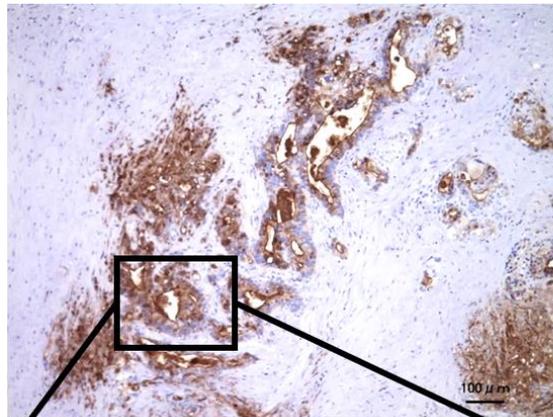


(RT-qPCR ; relative to GAPDH)

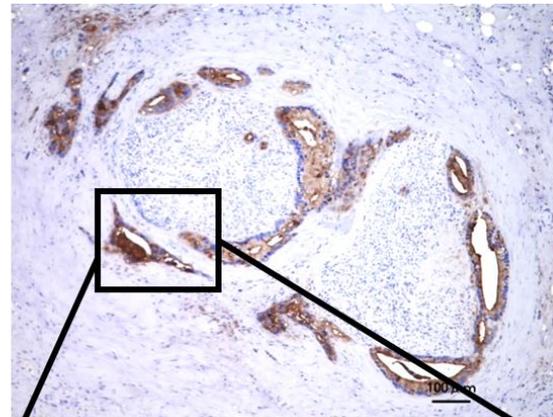


# rBC2LCN lectin identified as responsive to clinical pancreatic cancer

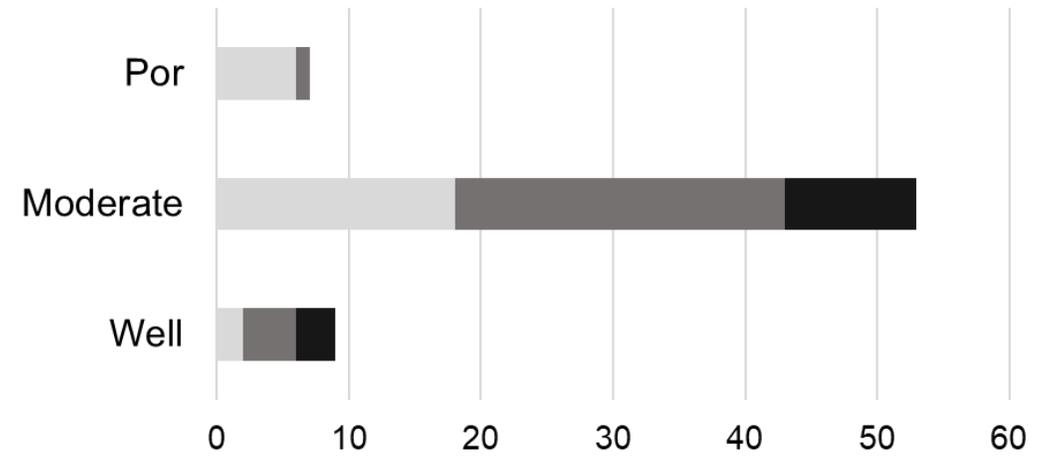
CASE1



CASE2



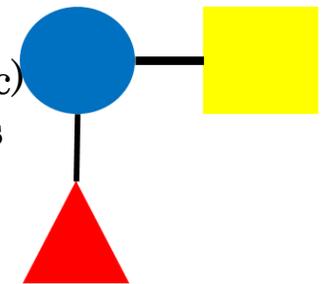
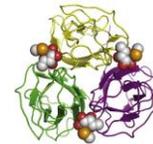
All positive in 69/69 cases



Recognize H type 1/3/4 structure

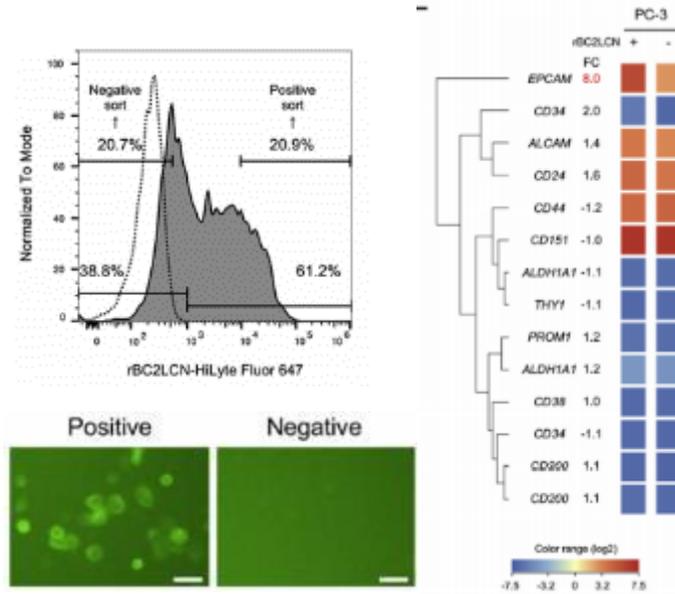
Fuca1-2Galβ1-3(GlcNac or GalNAc or Glc)  
H type 1, Lewis b and Lewis Y sequences

A



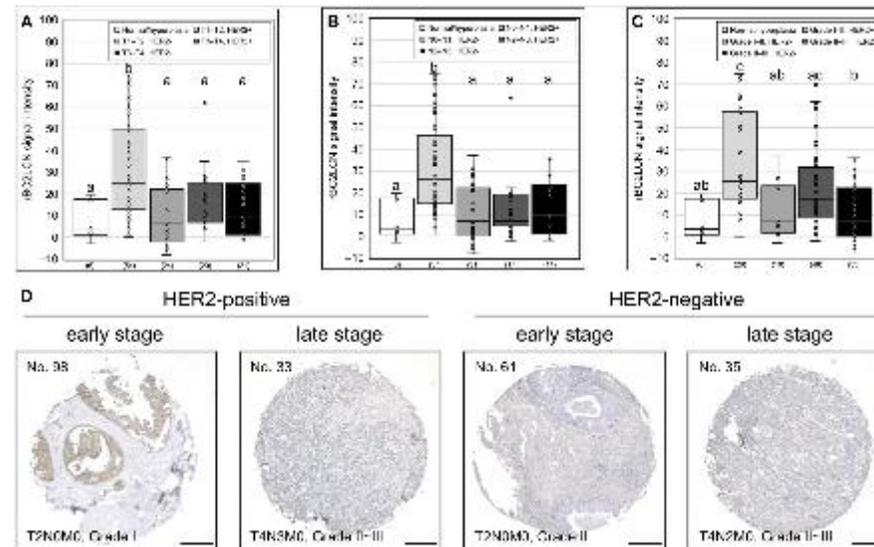
# rBC2LCN lectin reactivity in other cancer types

## Prostate cancer



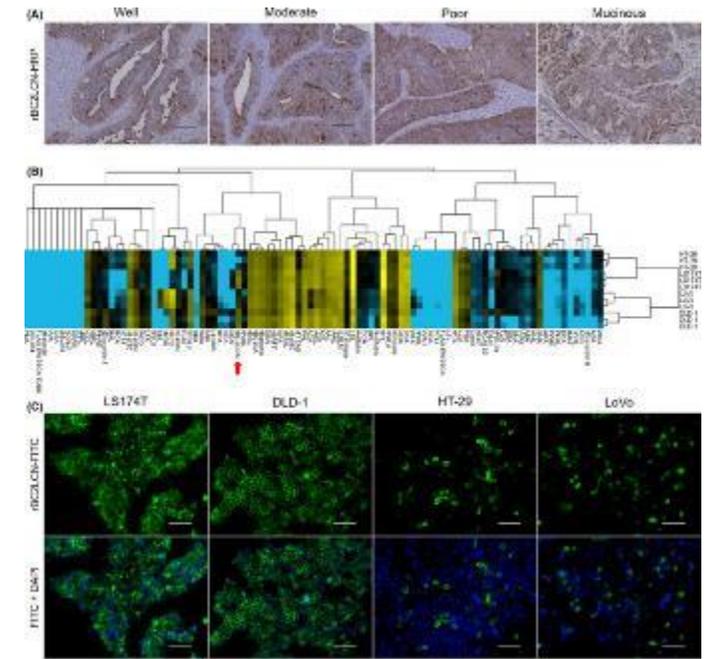
Mawaribuchi et al. BBRC 2019

## Breast Cancer



Mawaribuchi et al. FEBS open bio. 2020

## Colon cancer

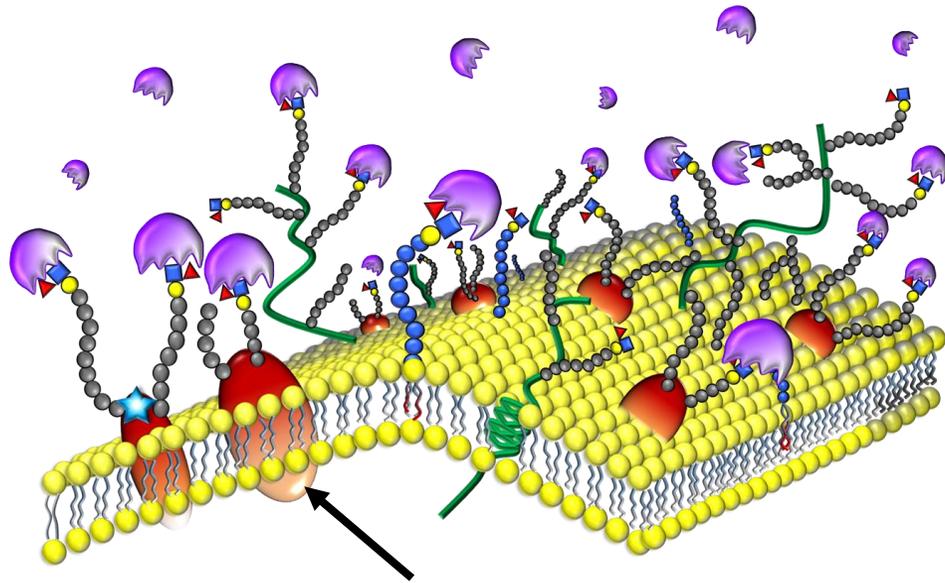


Kitaguchi et al. Cancer sci. 2020



# Searching for rBC2LCN positive core-protein in PDAC cells

Furuta T, Shimomura O, Tateno H et al., Cancer Science 2021



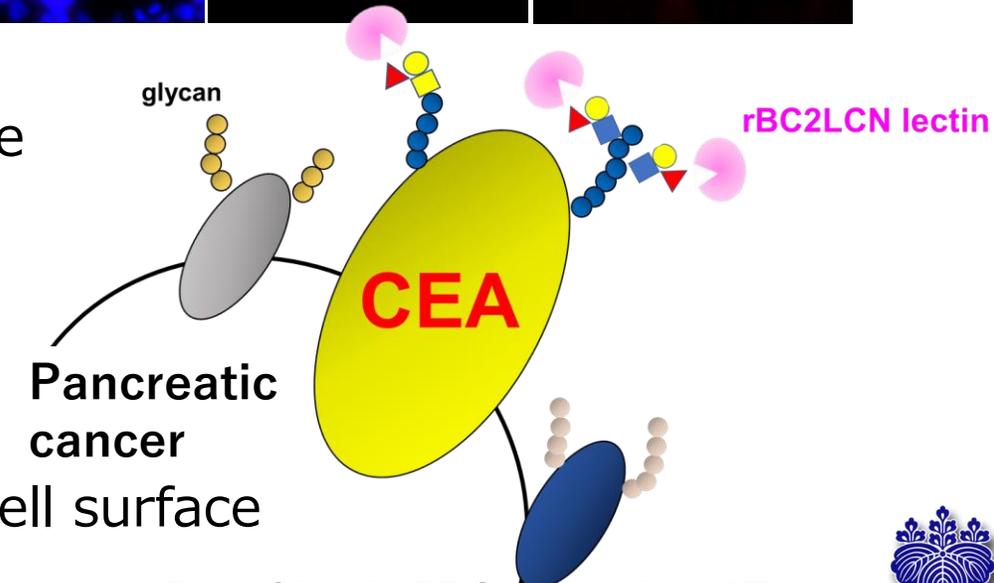
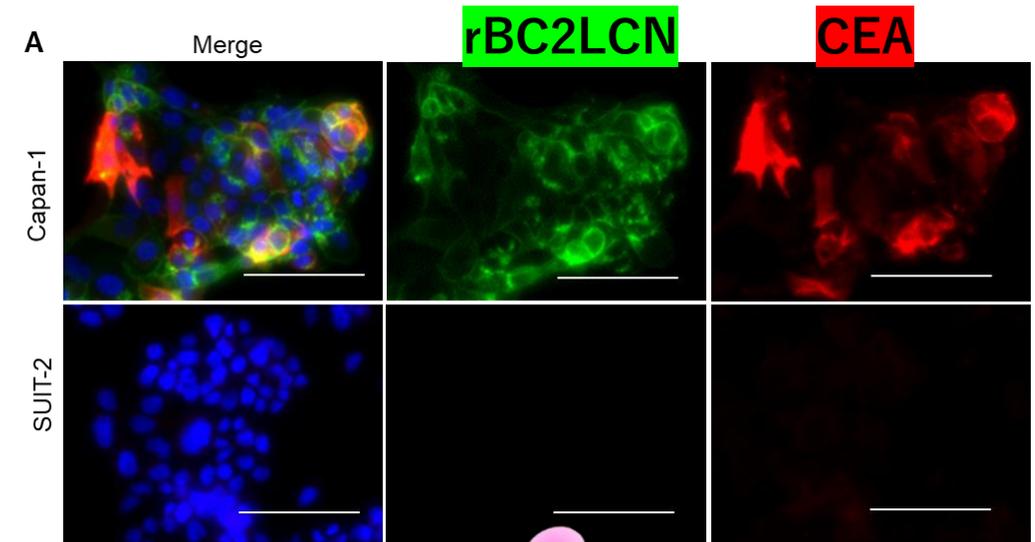
**Core-protein??**

Extract rBC2LCN positive fraction from PDAC cell lysate



By proteomics analysis, 40 candidates were found

➔ CEA is the most significant core-protein in PDAC cell surface



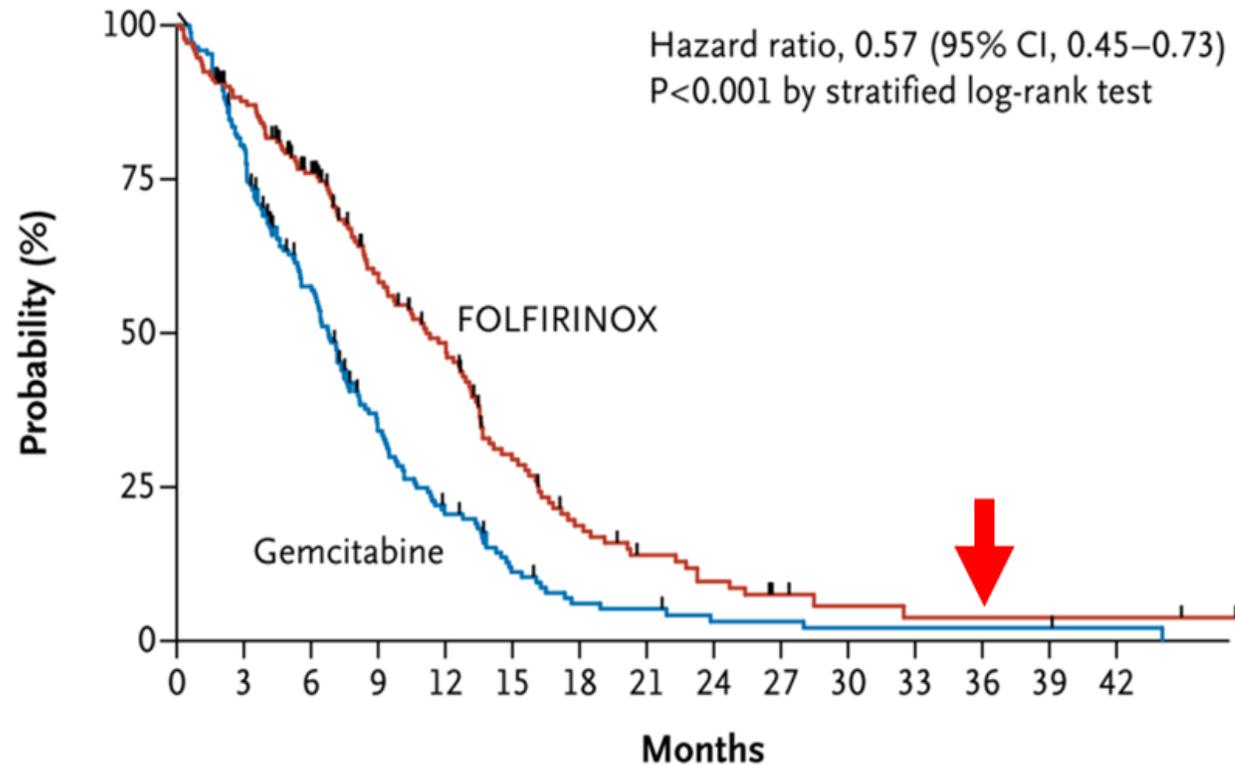
# Contents

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# Systemic chemoTx for metastatic PDAC

## FOLFIRINOX for Stage 4 pancreatic cancer



ACCORD11 trial

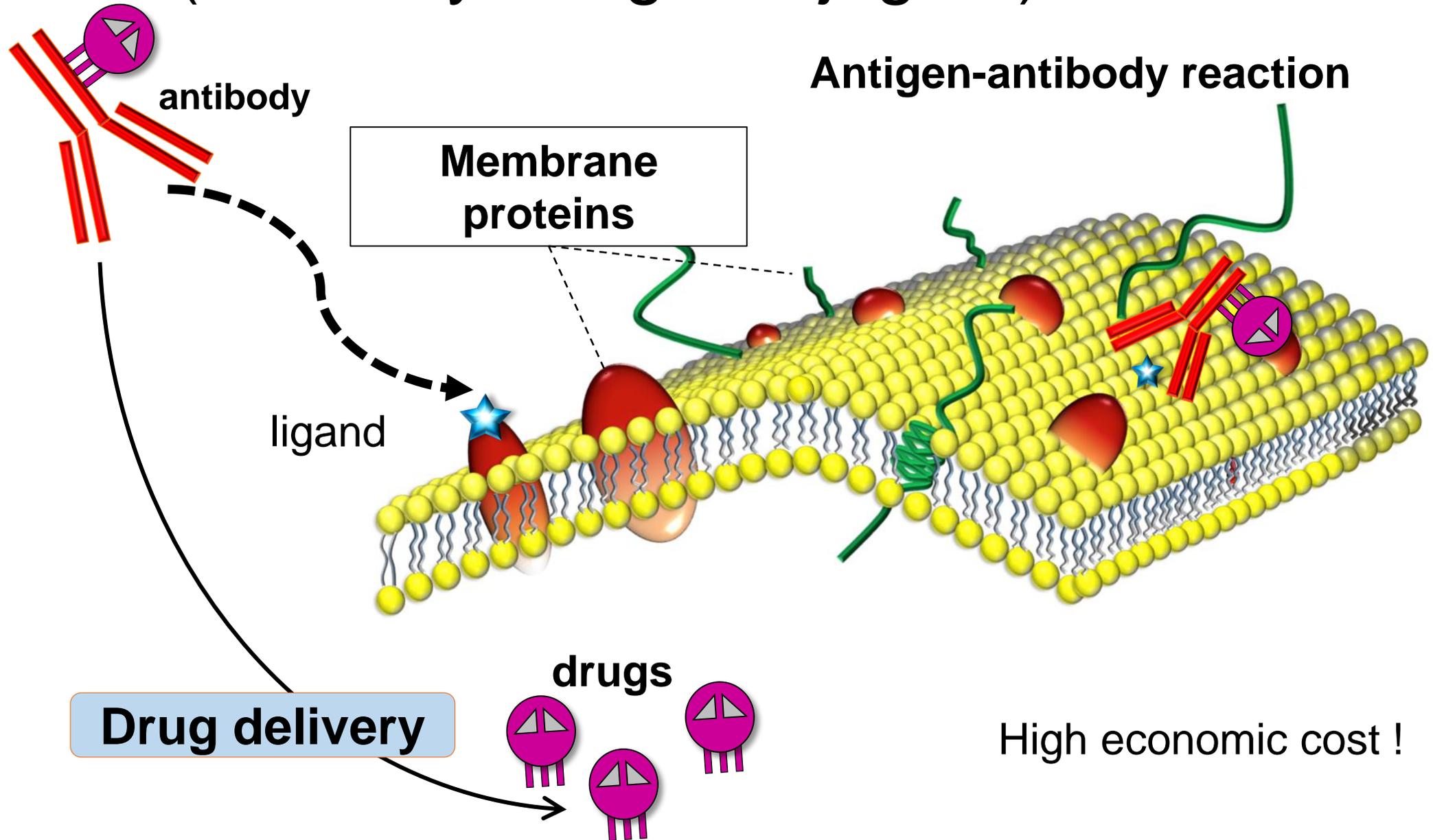
Conroy, T., et al. *N Engl J Med* 2011

**survival (median)  
11.1 months**

**3y survival ≐ 0%**



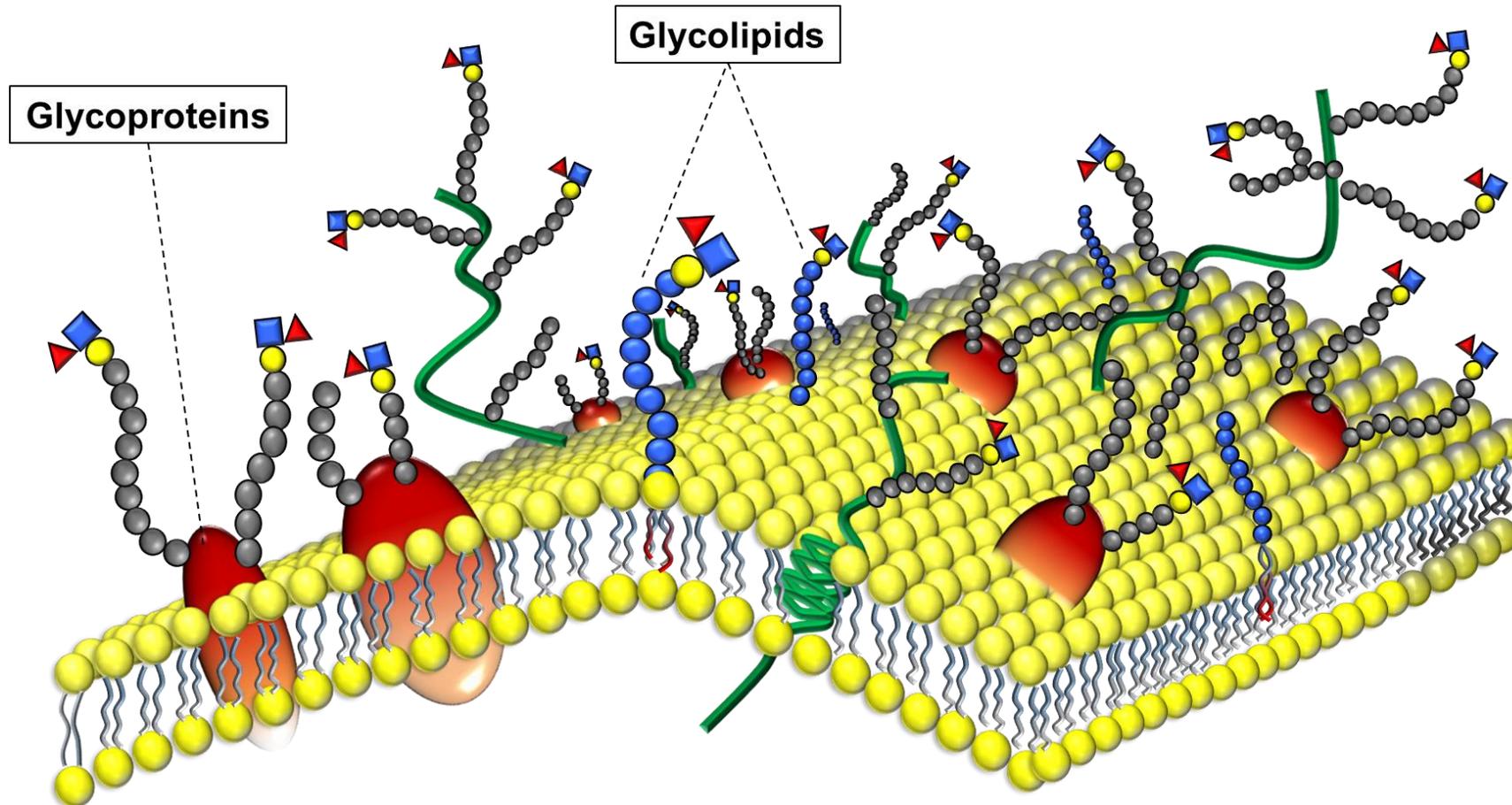
# ADC (Antibody-Drug Conjugate)



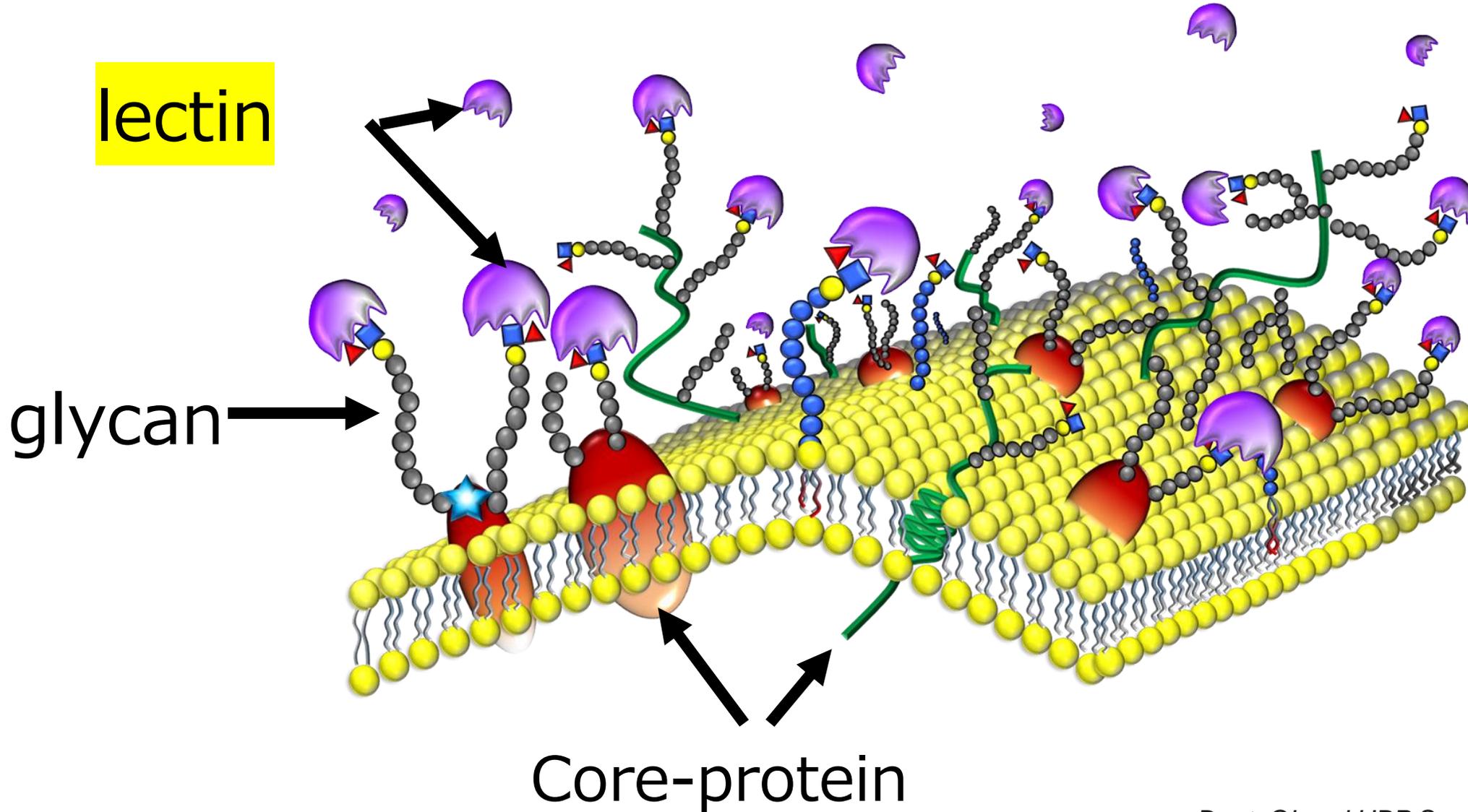
High economic cost !



# Is the cancer specific glycans are the target of molecular therapy??

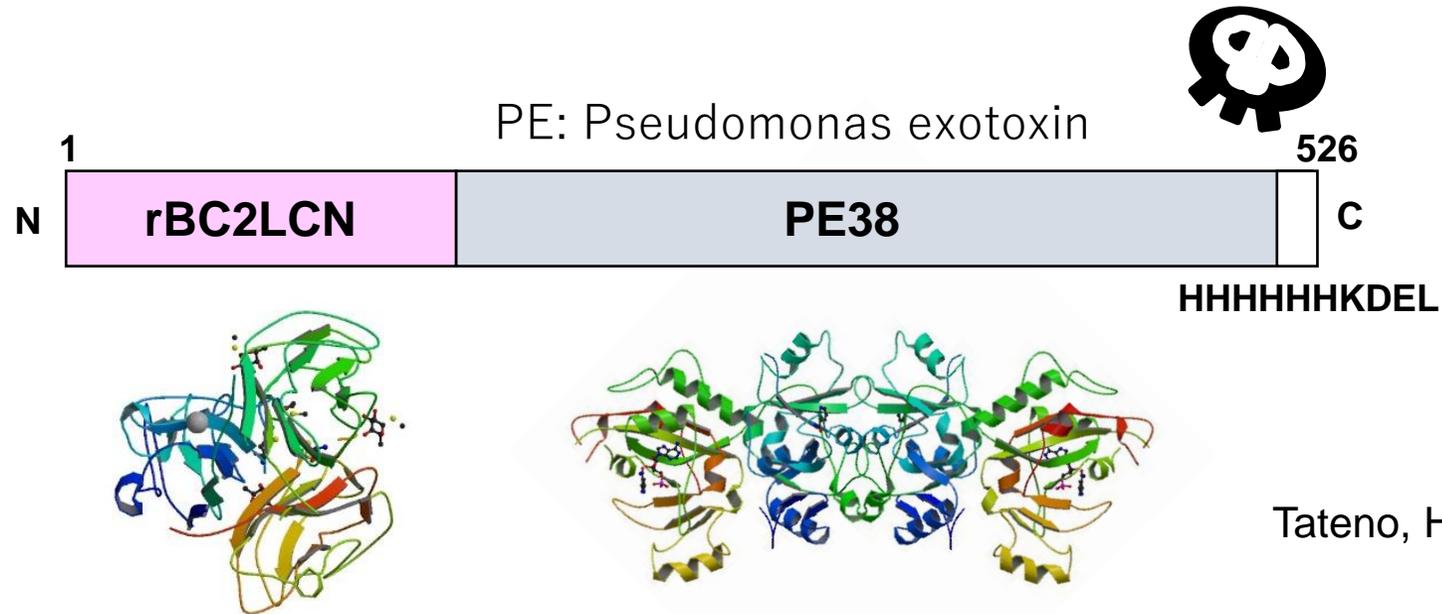


# “Lectins” may be a potential drug carrier



# Preparing the lectin—drug fusion drug

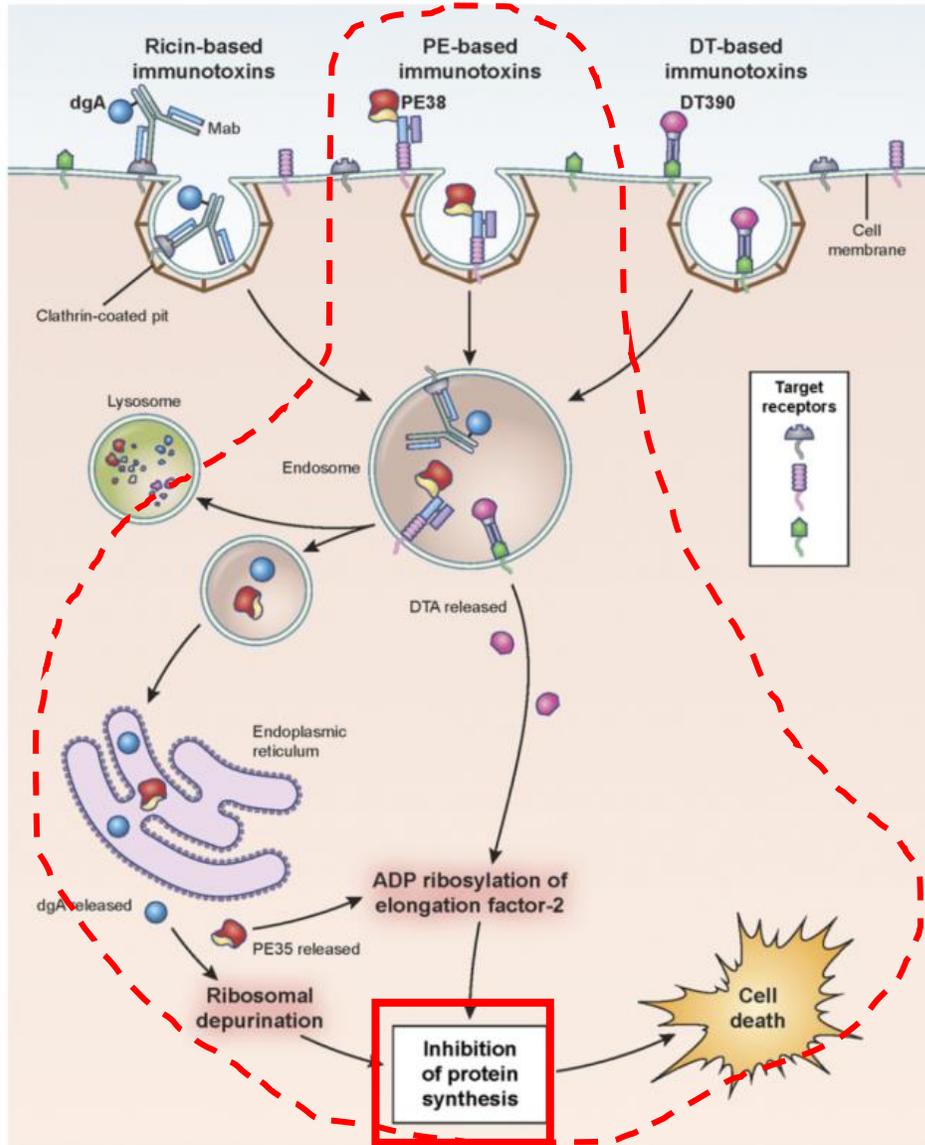
Lectin-Drug Conjugate “LDC” ( rBC2LCN-PE conjugate)



Synthesized fusion protein in E.coli system



# Pseudomonas aeruginosa Exotoxin A (PEA)



PE based Antibody-Drug Conjugate(ADC)  
Cytotoxic effect by inhibition of protein synthesis

Binding to membrane protein  
↓  
Internalized by endosome  
↓  
Transport to ER and released PE35  
↓  
elongation Factor-2 (ADP ribosylation)  
↓  
**Inhibition of protein synthesis**  
↓  
Cell death

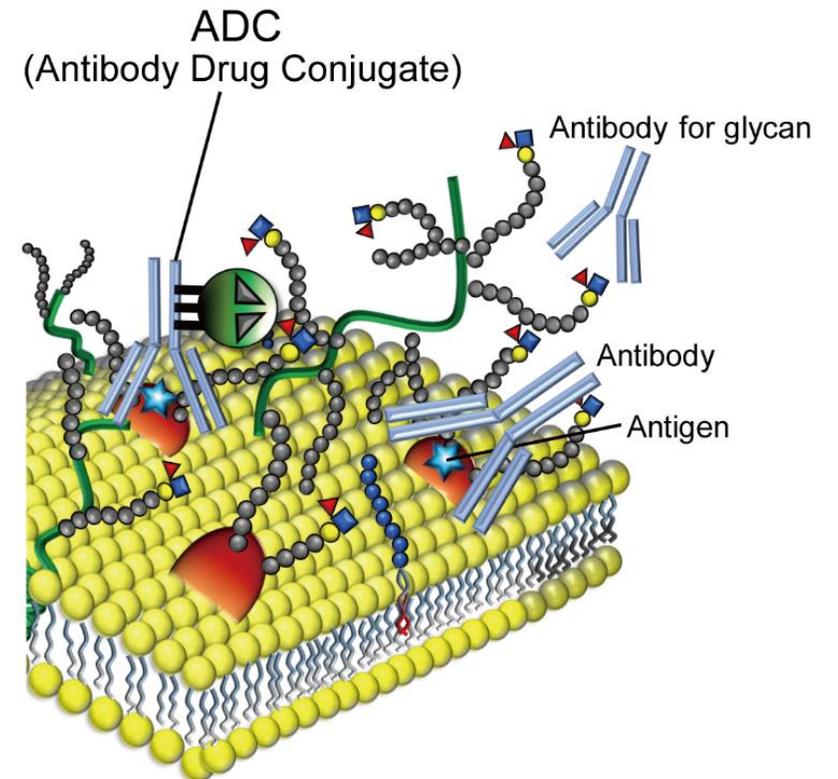


# Lumoxiti (Moxetumomab pasudotox-tdfk)

Anti-CD22 antibody-PE38 (FDA approval 2018/9/13)

ADC (Antibody-drug conjugate)

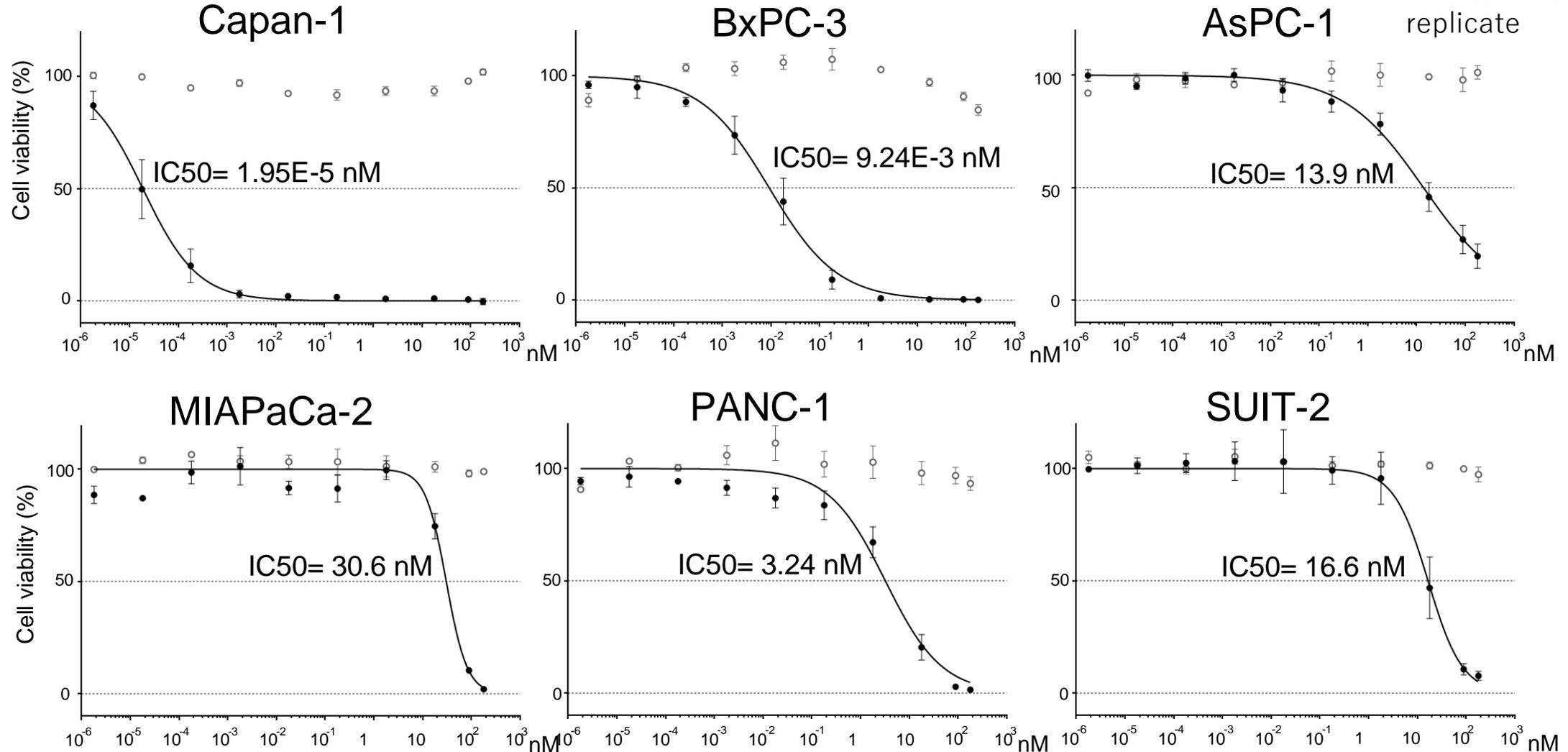
→ refract hairy cell leukemia



# LDC (rBC2LCN-PE38) cytotoxic effect MTT (WST-8 test)

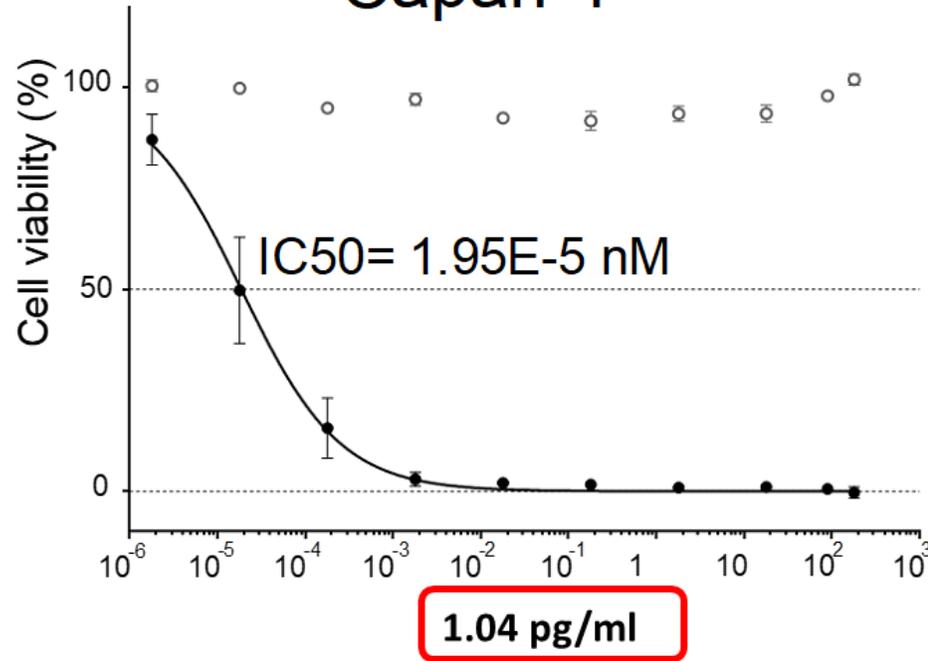
○ : rBC2LCN only    ● : rBC2LCN-PE38

n=3 technical replicate

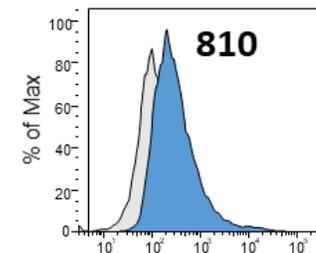
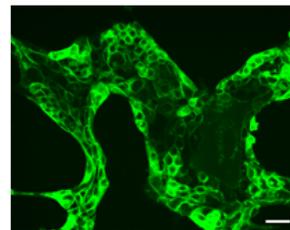
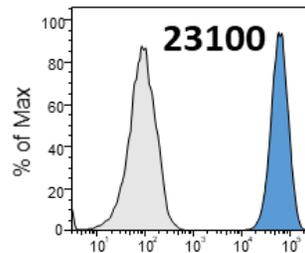
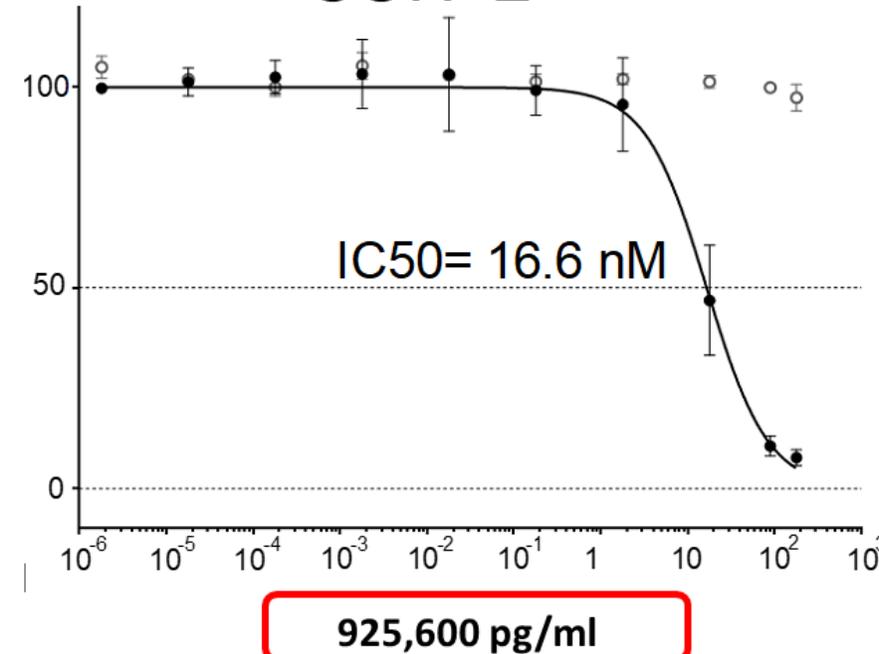


# LDC (BC2-PE38) for pancreatic cancer

Target glycan +  
Capan-1



Target glycan -  
SUIT-2



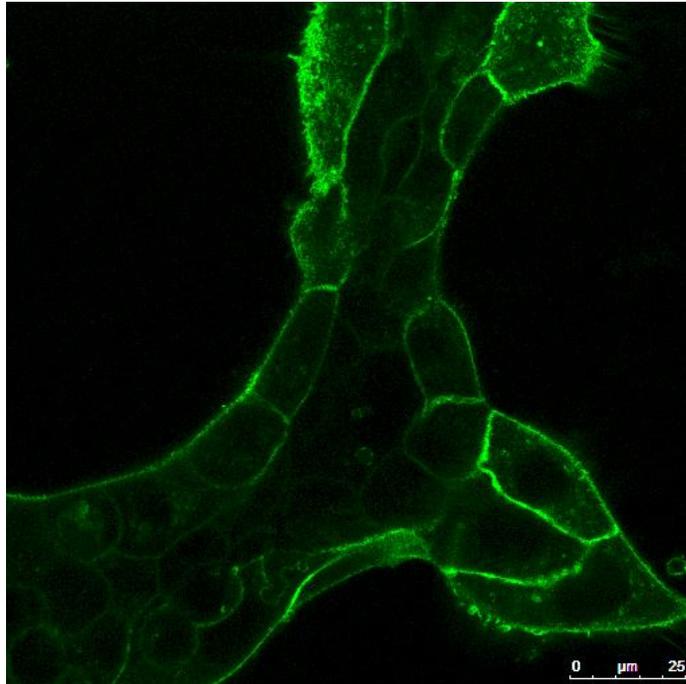
**IC50= 1.04pg/ml** for Capan-1 (Target glycan + cells)



# Internalization of rBC2 lectin to Capan-1

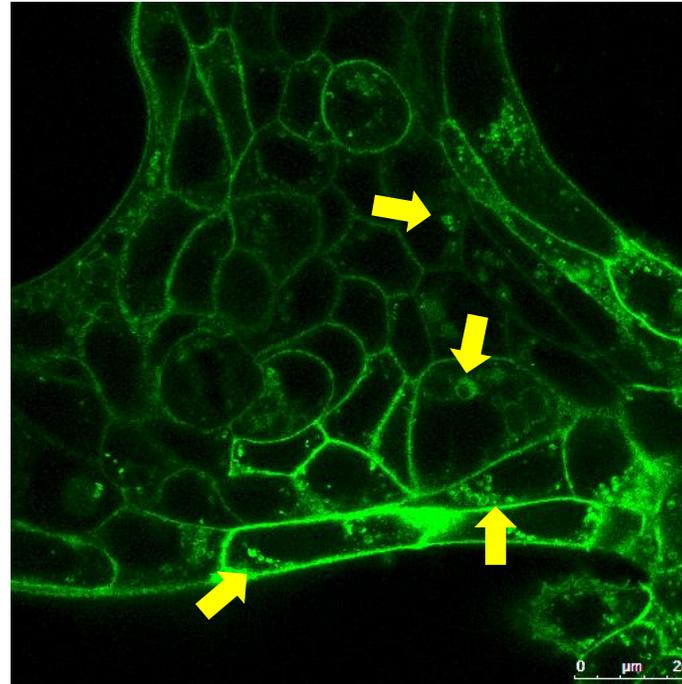
Green: rBC2LCN-FITC

1 Hour



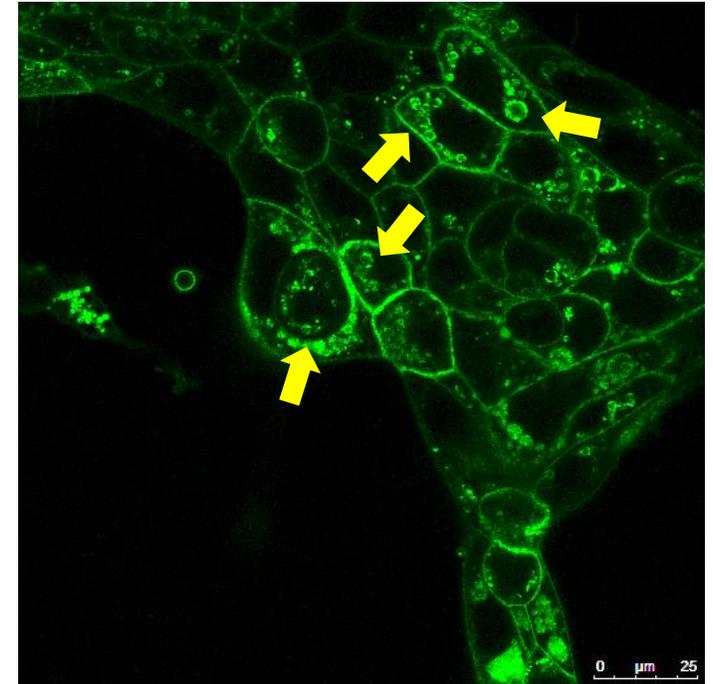
Bind to cell surface

24 Hour



lectins was detected inside the cell

48 Hour



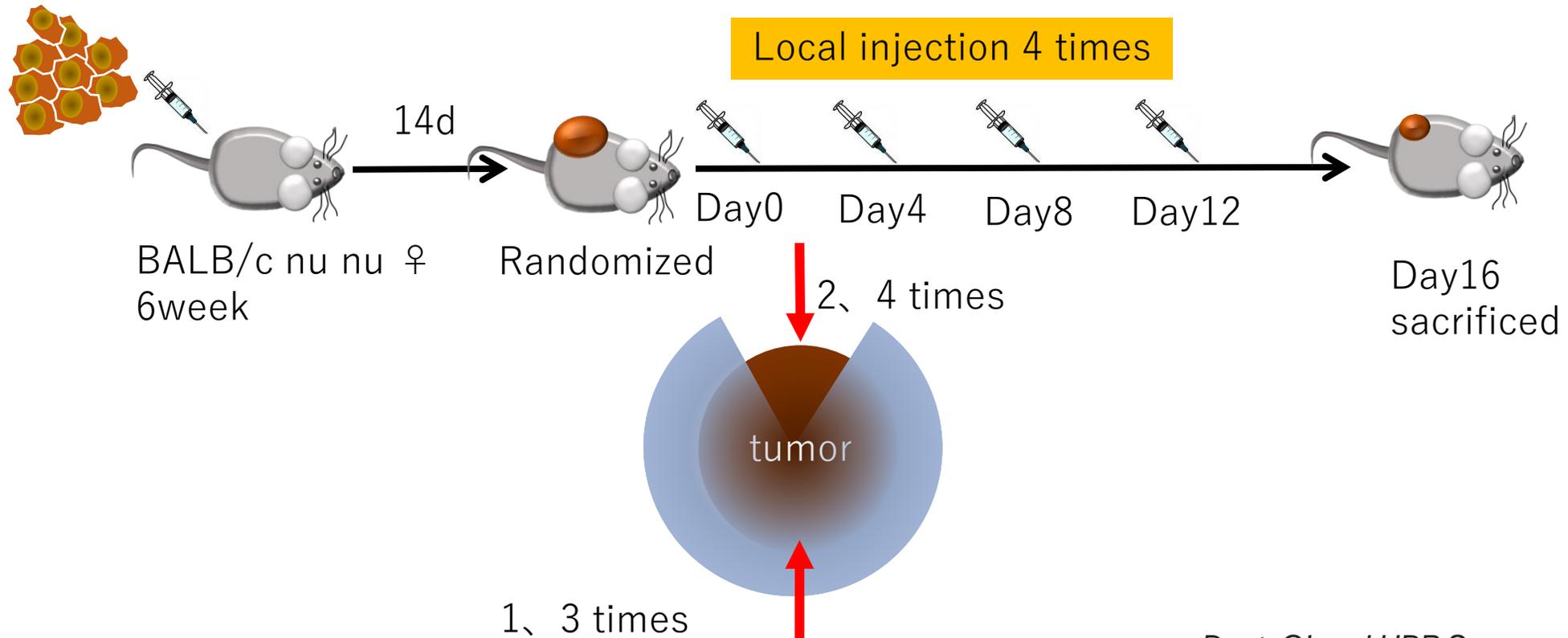
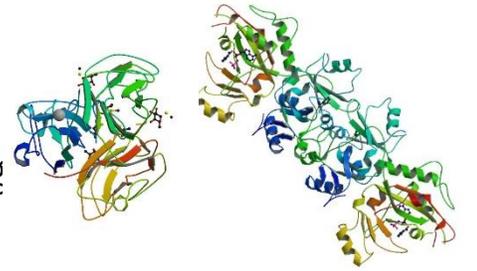
The amount of lectin increased



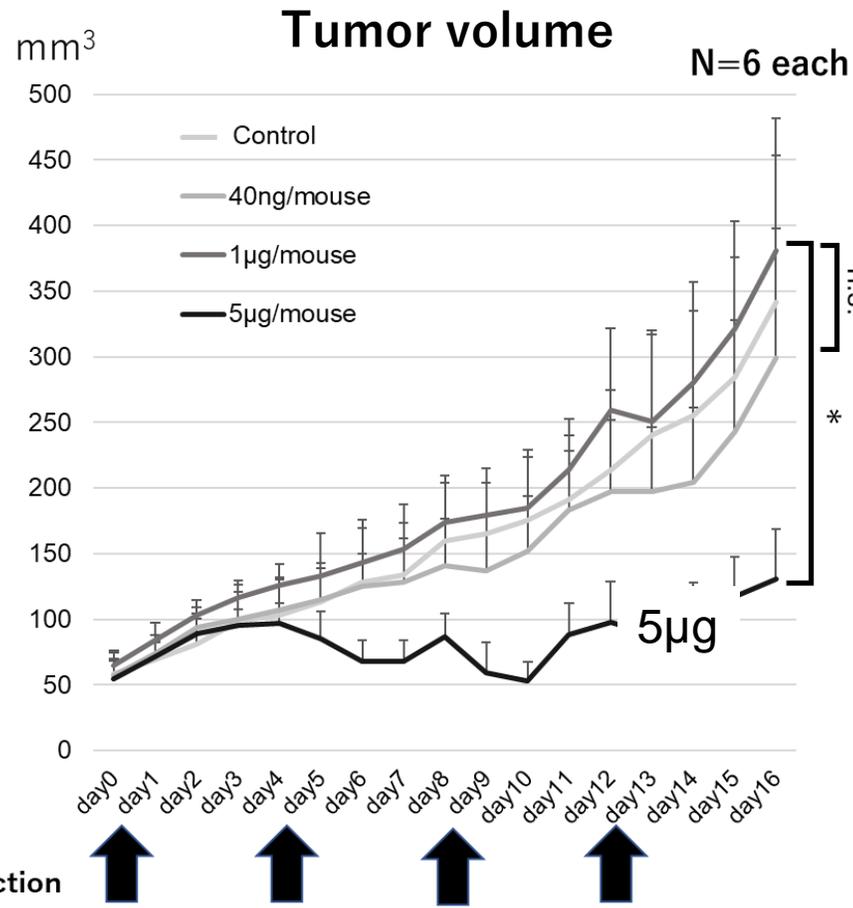
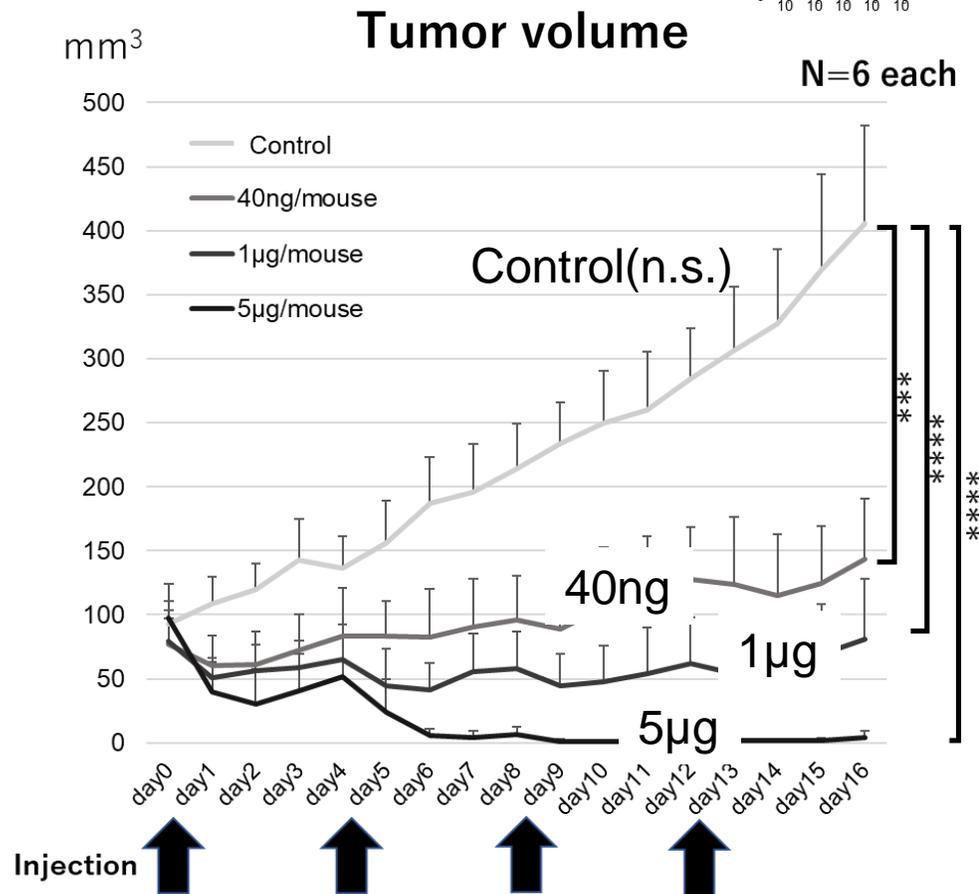
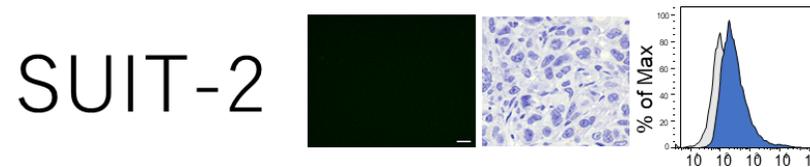
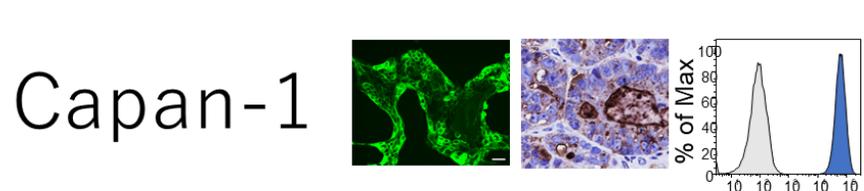
# Lectin Drug Conjugate for PDAC cell xenograft

Capan-1, SUIT-2  
2M S.C

N=6 {  
0: Control (normal saline) 100μl  
1: LDC 40ng/100μl /body (2μg/kg)  
2: LDC 1μg/100μl /body  
3: LDC 5μg/100μl /body



# Lectin Drug Conjugate for PDAC cell xenograft



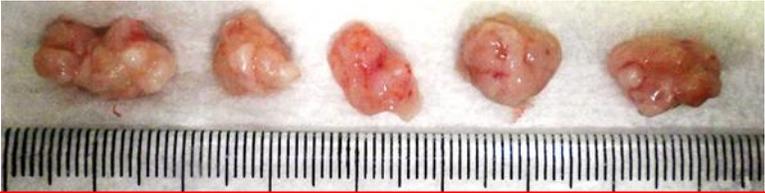
N=6 biological replicate \* : P<0.05, \*\*\*:P<0.001, \*\*\*\*:P<0.0001 n.s.: not significant Relative to control



# Lectin Drug Conjugate for PDAC patient derived xenograft

Pancreas tumor

Control



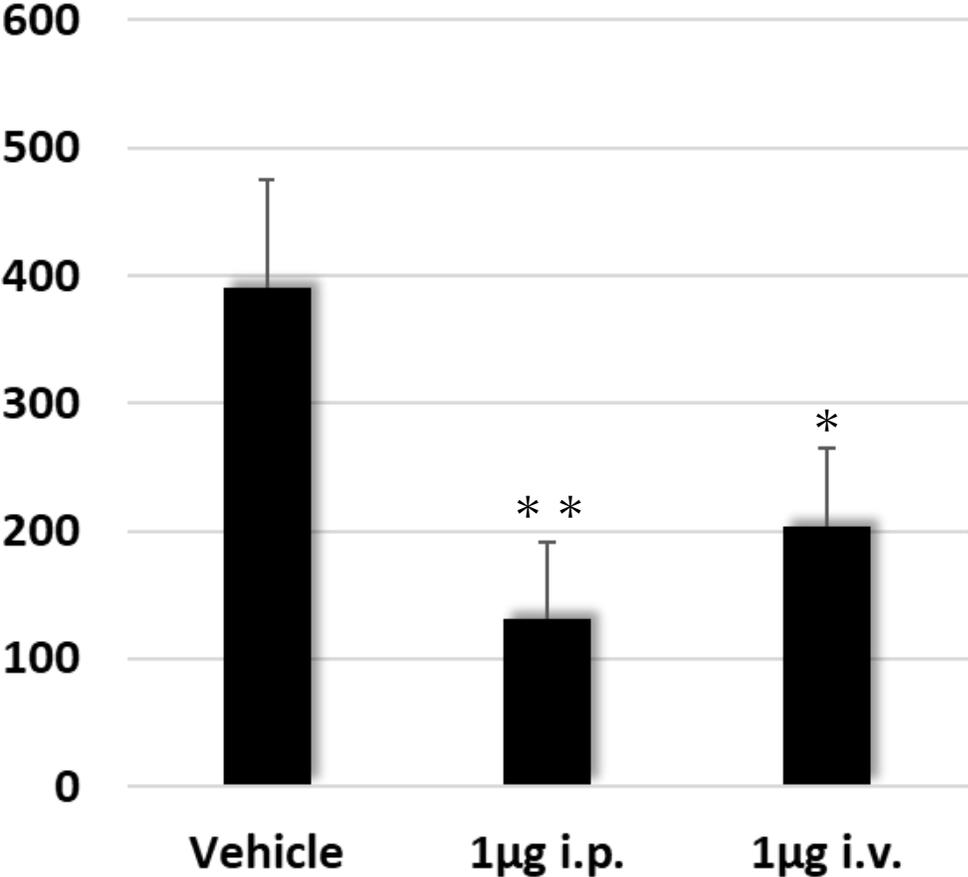
LDC 1ug i.p.



LDC 1ug i.v.



## Tumor weight



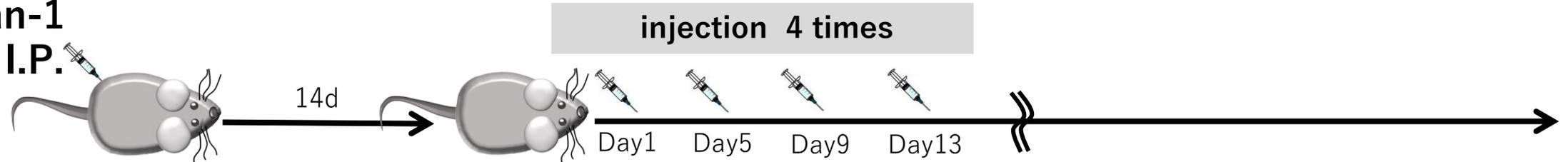
	Dissemination	Liver Metastasis	Spleen Metastasis
Vehicle	4	4	3
1µg i.p.	0	0	1
1µg i.v.	1	0	2

N=5 biological replicate  
 \*: P<0.05, \*\*:P<0.01  
 Relative to control by ANOVA  
 (Turkey)

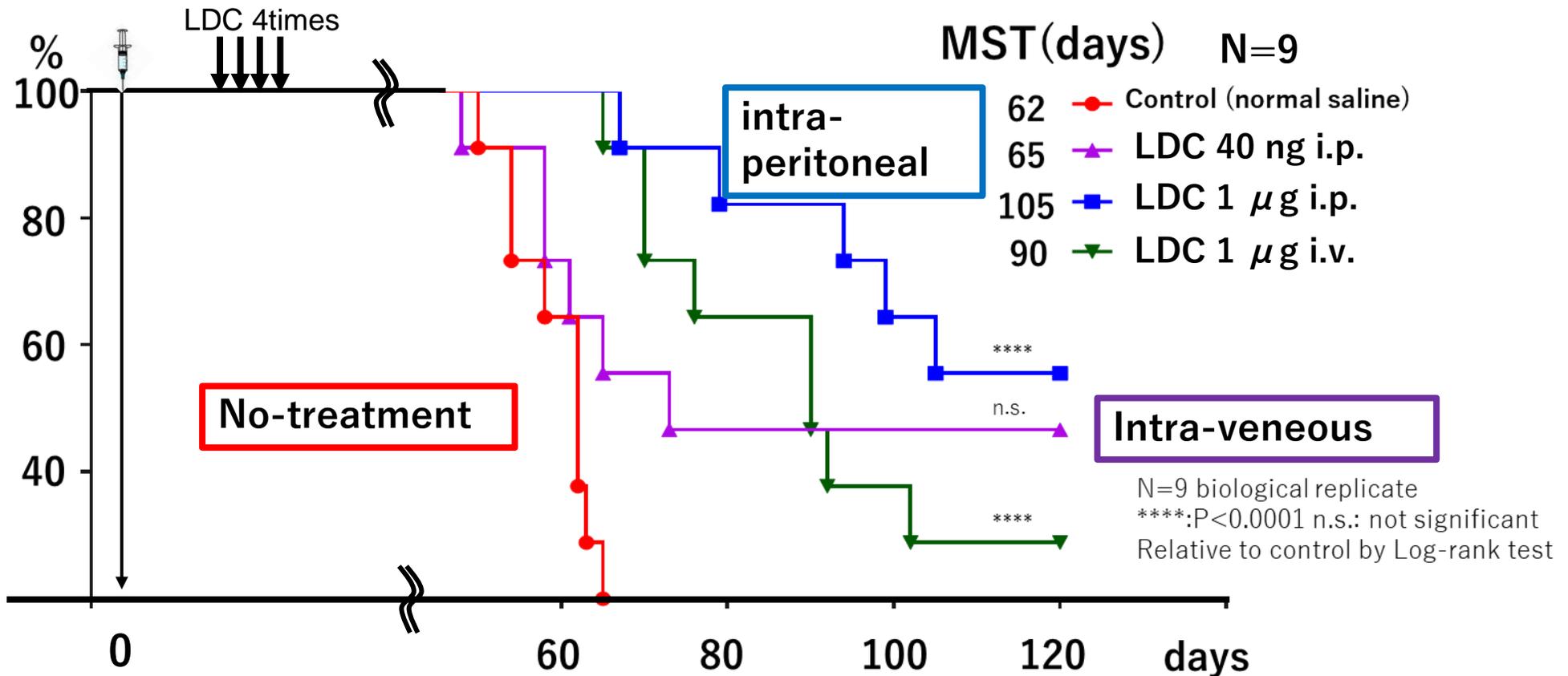


# Improve dissemination models by 4 times LDC injection

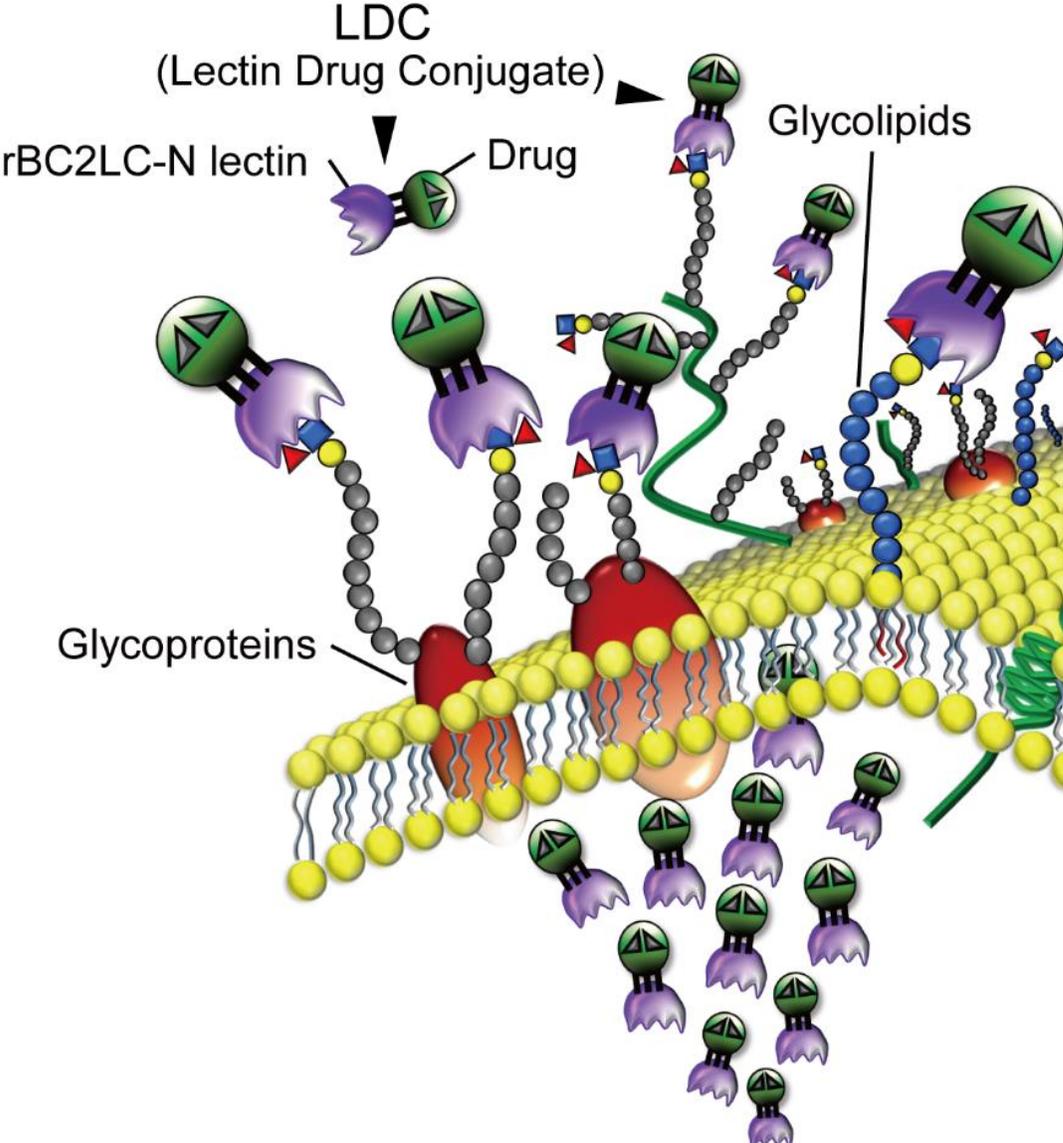
Capan-1  
2M I.P.



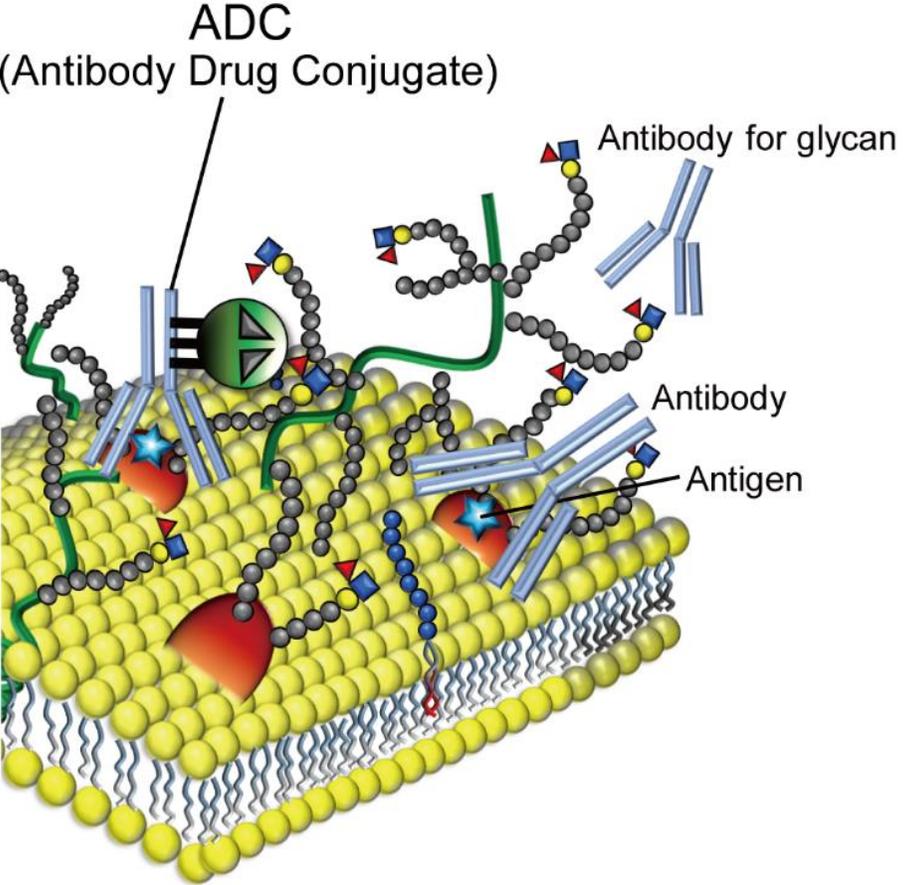
BALB/c nu nu ♀ 6week



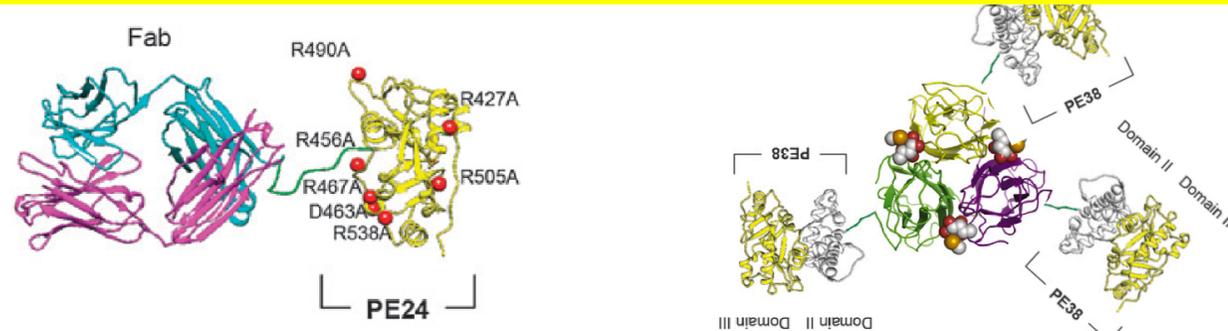
# Drug delivery by “lectin”



# Drug delivery by “antibody”



# ADC vs. LDC for Pancreatic Cancer



	RG7787	LDC
Institution	The U.S. NCI (Ira Pastan et al.)	Japan AIST-Tsukuba
Targeting bullet	Fab of antibody	rBC2LC-N lectin
Target	Mesothelin	H type 1,3,4 glycan
Payload	PE24	PE38
MW (kDa)	72	54 (162 at trimer)
Disease	Mesothelioma, Panc ca. (Ovarian ca., Lung ca., Gastric ca., Bile duct ca.)	Panc ca. (Ovarian ca., Lung adeno ca., Gastric ca., Colon ca.)
IC50 (ng/mL)	1.38	0.00104 (1.04 pg/ml)
(pmol/L)	18.9	0.0195 (=2 fmol/L)
LD 50 (mg/Kg)	10	0.36



# 1,000 times stronger than reported ADCs

Target antigen	malignancy	Agents name	Toxin	IC50	Reference
IL-2R	CLL	Anti-Tac(Fv)-PE40KDEL	PE	1.2~9 ng/ml	Kreitman, R. J., et al. 1992
GP185/HER2	Breast Ovary	Saporin Anti-GP185/HER2 IT	SAP	0.43~1.1 nM	Tecce, R., et al. 1993
IL-2R	ATL CLL	Anti-Tac(FV)-PE40	PE	0.04~ >1000 ng/ml	Kreitman, R. J., et al. 1994
NCAM	Lung cancer	SEN7-PE	PE	22~85 pM	Zangemeister, U., et al. 1994
CD80	Hodgikin's	Anti-B7-1-saporina	SAP	3.2 ng/ml	Vooijs, W. C., et al. 1997
GRP	Lung	DAB389GRP	DT	9.5 pM	vanderSpek, J. C., et al. 1997
E4	Prostate	E4PE35-KDEL	PE	0.3-20 ng/ml	Essand, M. and I. Pastan 1998
CD30	Hodgikin's	Ki-4(scFv)-ETA	PE	43 pM	Klimka, A., et al. 1999
CD22	lymphoma	RFB4(dsFv)-PE38	PE38	0.4 ng/ml	Kreitman, R. J., et al 1999
IL-13R	Head and Neck	IL13-PE38	PE38	3~7 ng/ml	Kawakami, K., et al. 2001
IL-4R	Pancreas	IL4-PE38	PE38	0.3~0.5 ng/ml	Kawakami, K., et al. 2002
EpCAM	Head and Neck	4D5MOCB-ETA	PE	0.005~0.2 pM	Di Paolo, C., et al. 2003
GCSF	AML	DTU2GSF	DT	5.8~34.7 pM	Abi-Habib, R. J., et al. 2004
CD19	Blood	FMC63(Fv)-PE38	PE38	0.6-14 ng/ml	Du, X., et al. 2008
CD22	Blood	RFB4(Fv)-PE38	PE38	50-550 ng/ml	Du, X., et al. 2008
CD22	Blood	B3(dsFv)-PE38	PE38	0.1-2.5 ng/ml	Weldon, J. E., et al. 2009
CD30	Lymphoma	SGN-35	MMAE	1.3 ng/ml	Okeley, N. M., et al. 2010
mesothelin	Pancreas	RG7787	PE24	1.38~33.28 ng/ml	Hollevoet, K., et al. 2014
HER2	Breast	4D5scFv-ETA	PE40	22 nM	Sokolova, E. A., et al. 2014
CD71	Pancreas	HB21(Fv)-PE40	PE40	3~3.7 ng/ml	Hollevoet, K., et al. 2015
Glypican-3	liver	HN3-PE38	PE38	0.068 nM~	Gao, W., et al. 2015
<b>H type 1/3/4</b>	<b>Pancreas</b>	<b>rBC2-PE38</b>	<b>PE38</b>	<b>1.04 pg/ml (0.0195 pM)</b>	<b>Author</b>

ADCs

IC50 = 1~1000 ng/ml

1,000~  
10,000  
Times

LDC: IC50 = 1.04 pg/ml

CLL; chronic lymphocytic leukemia, ATL: adult T-cell leukemia, PE; pseudomonas aeruginosa exotoxin, DT; diphtheria toxin, SAP; plant toxin saporin 6, MMAE; monomethylauristatin E,

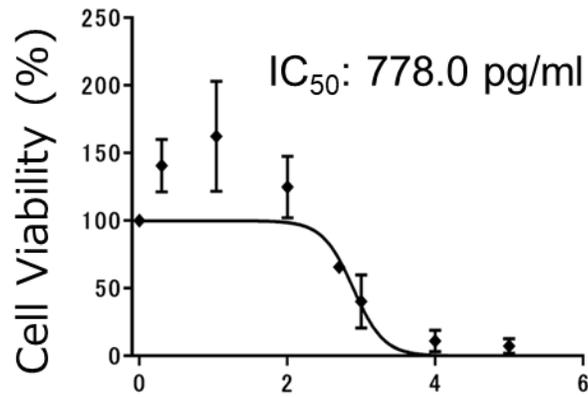


# LDC for other cancer types

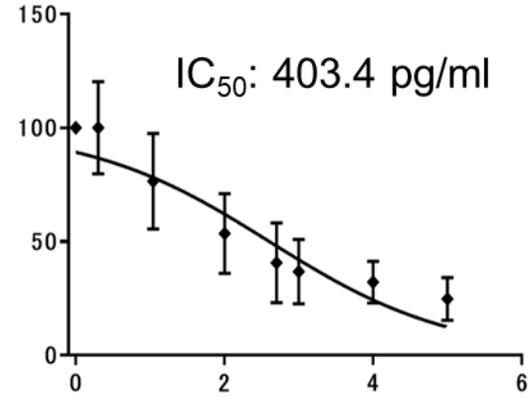
Stomach, Colon cancer



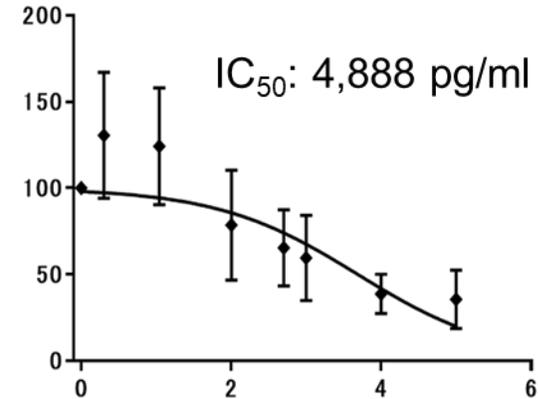
# LDC (BC2-PE38) for colon ca. cell lines



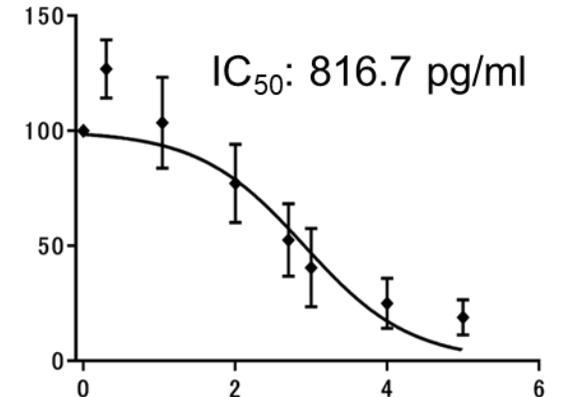
**LS174T**



**DLD-1**

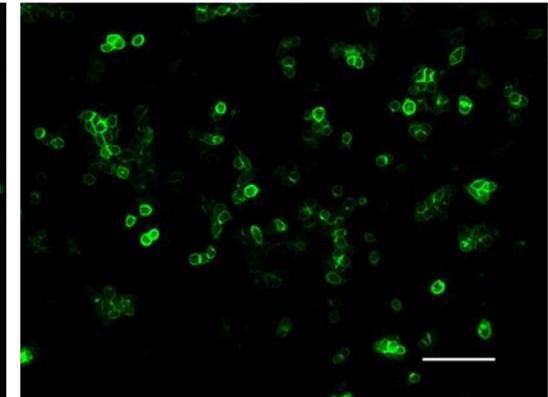
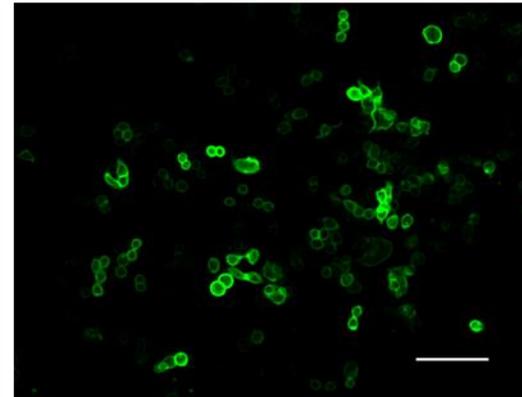
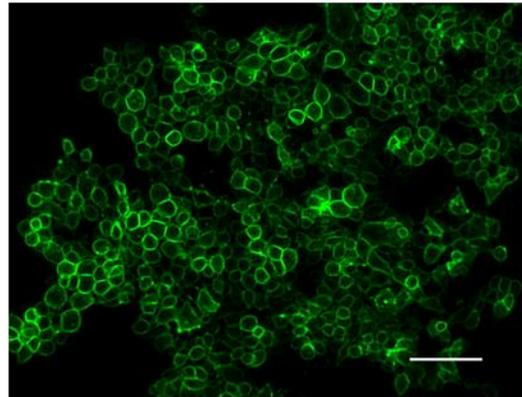
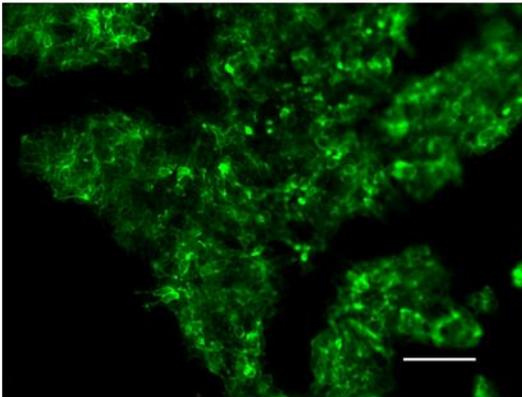


**HT-29**



**LoVo**

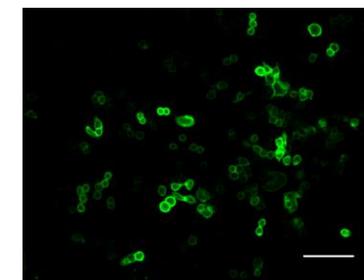
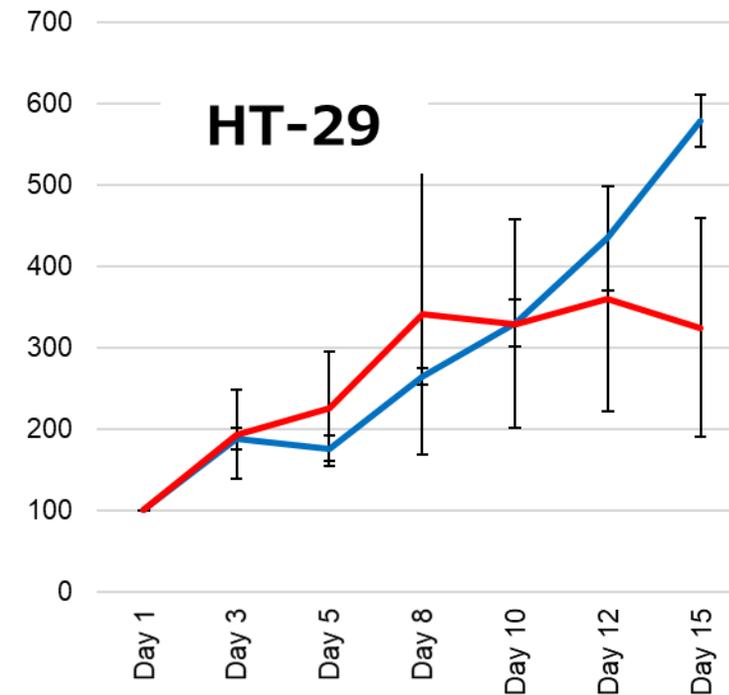
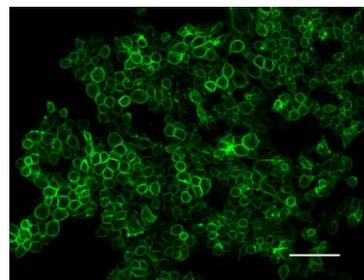
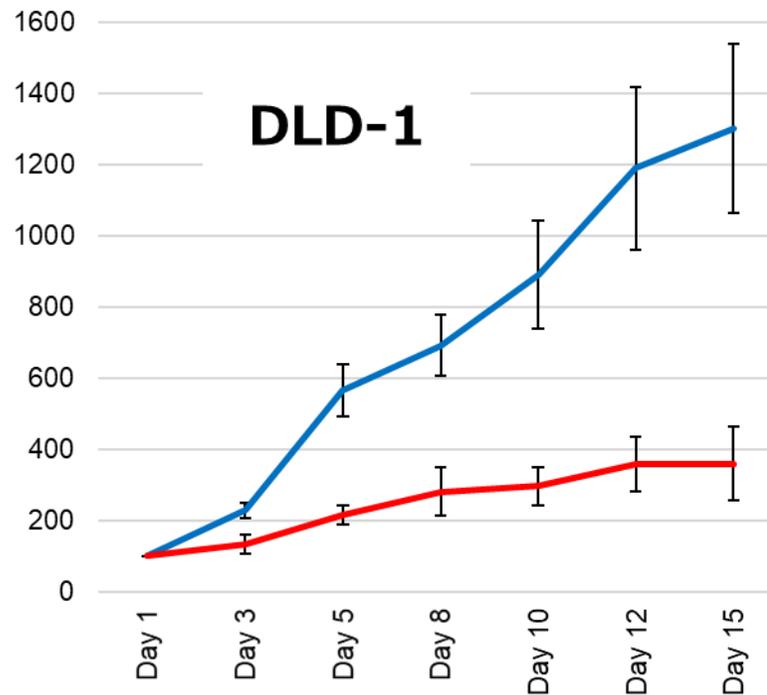
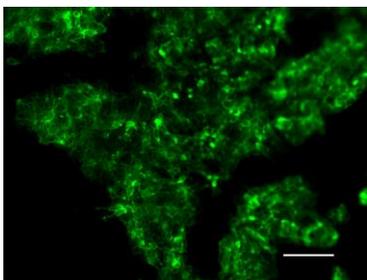
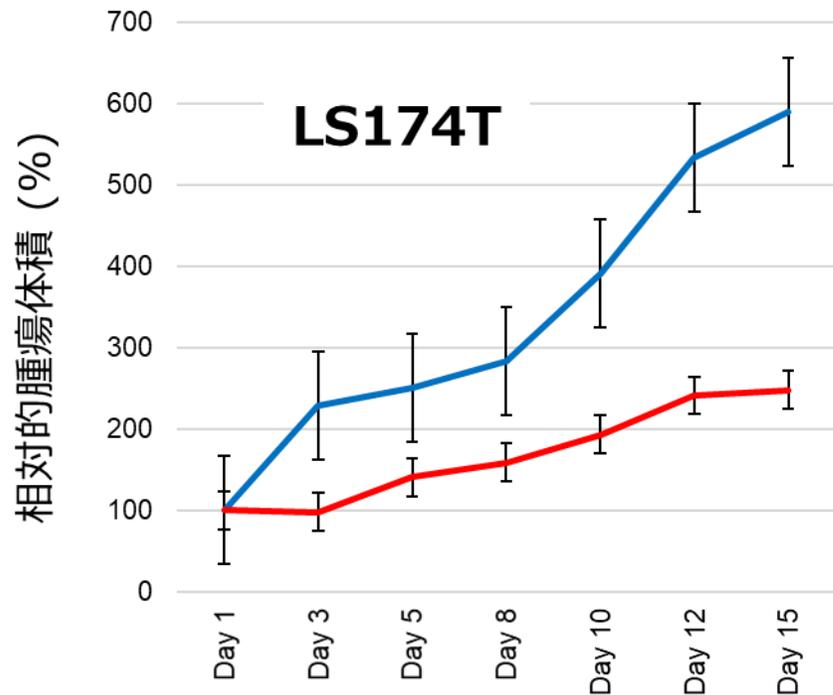
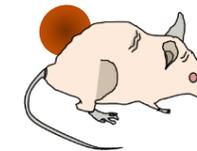
rBC2LCN-FITC



Kitaguchi D, Shimomura O, Tateno H et al., Cancer Science 2020



# rBC2LCN-PE38 effect for colon ca. xenograft models



# LDC anti-cancer effect for colon cancer

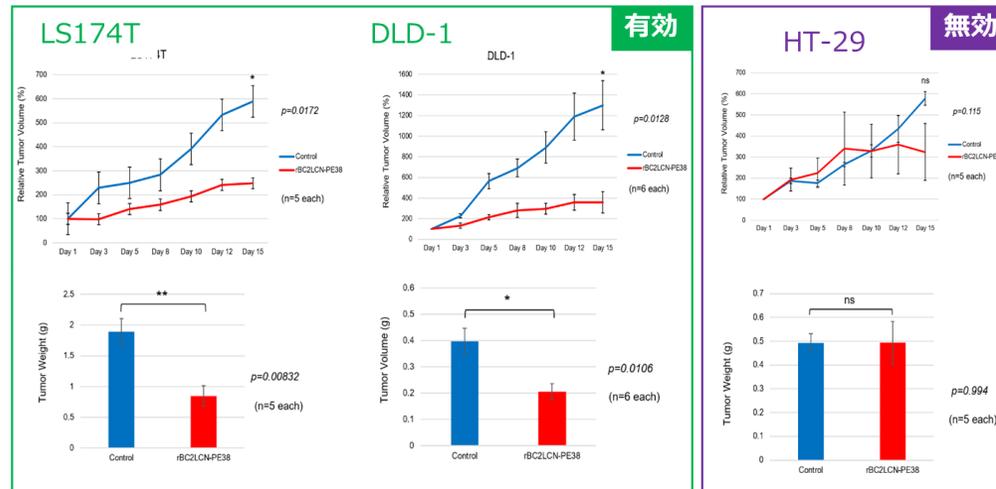
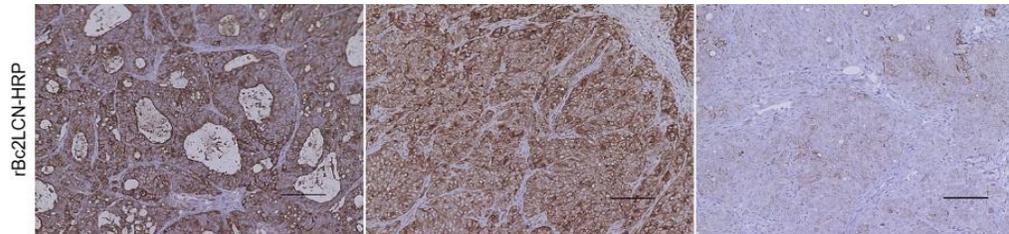
Evaluate the LDC effect to colon ca. cell lines

LS174T

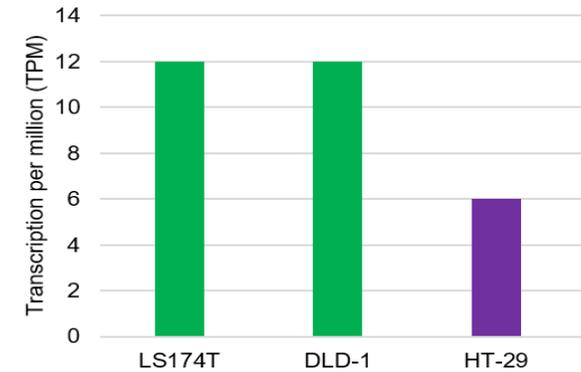
DLD-1

HT-29

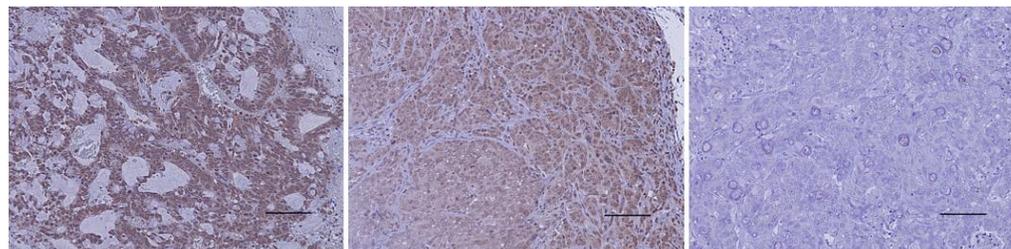
Kitaguchi, Shimomura, Oda, et al., Cancer Science 2020



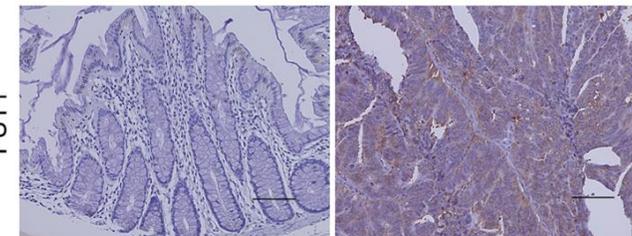
FUT1 Fcosyltransferase qPCR



FUT1 Expression



Human Normal Human Cancer



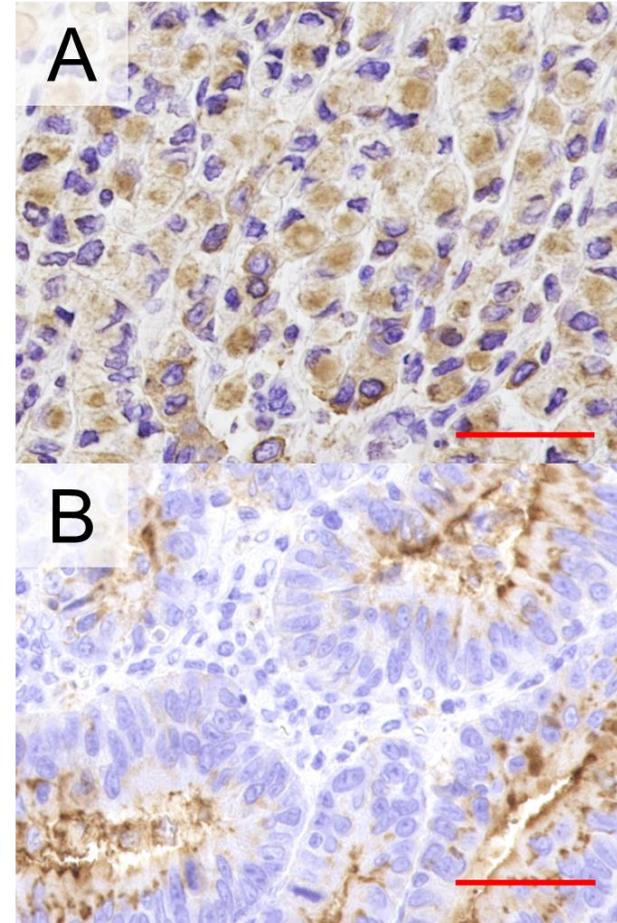
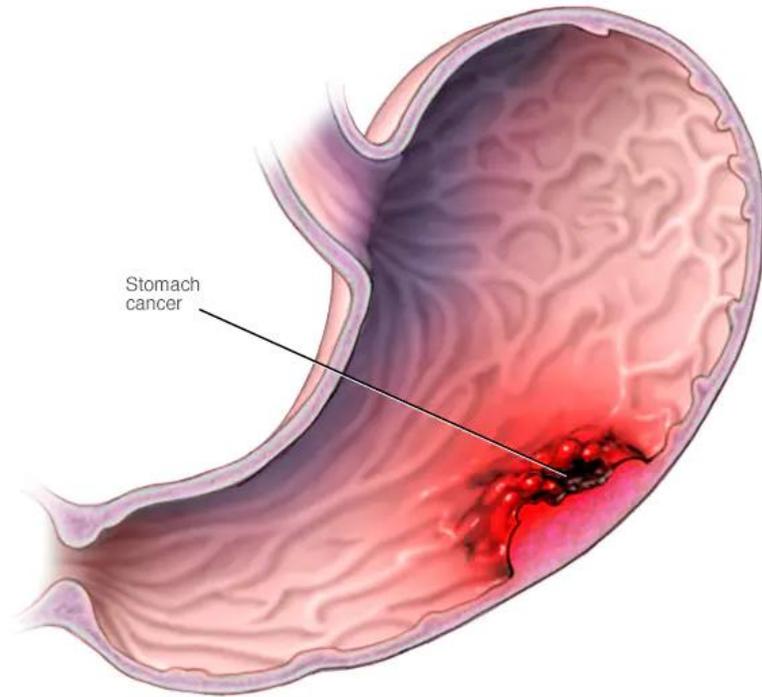
Normal < Tumor

Significant difference in FUT1 expression

Dept. GI and HBP Surgery, Univ of Tsukuba



# LDC effect for stomach cancer



Scirrhus Type

Mordareteley  
differentiated

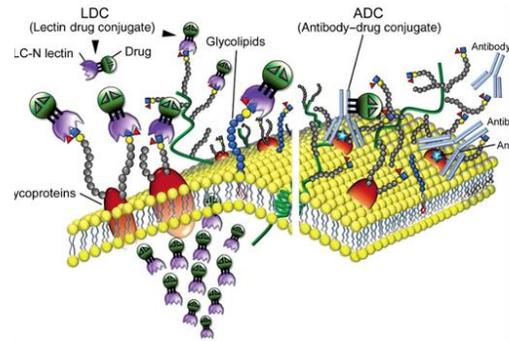
rBC2LCN lectin-HRP

Yang Y, Akashi Y, Shimomura O, Tateno H, *et al*: Gastric Cancer 2022



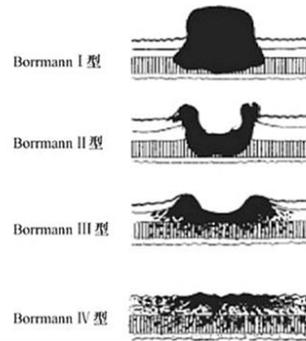
# Evaluate the effect of LDC to stomach cancer

## Is lectin a potential drug carrier for GC?



—A Novel Therapeutic Strategy for Pancreatic Cancer: Targeting Cell Surface Glycan Using rBC2LC-N Lectin-Drug Conjugate (LDC). O. Shimomura. *Mol Cancer Ther*. 17(1): 183-95. ©2017 AACR

Apply to GC?



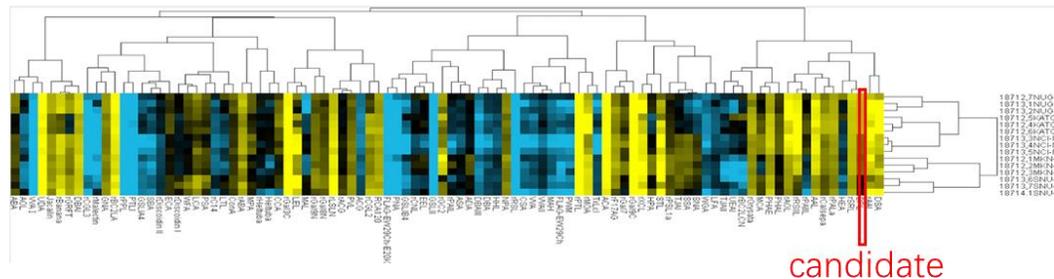
method



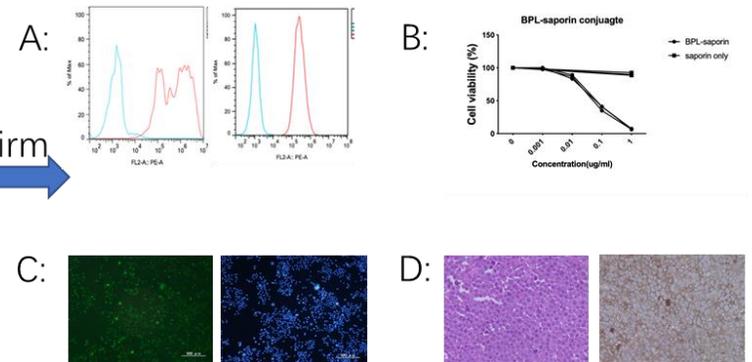
- Protein extraction
- Lectin array: find the lectin
- Lectin blotting: check the affinity
- FACS: check the affinity of cell lines
- Lectin staining
- MTT assay
- Hemagglutination
- Check in vivo

Aim: To develop a novel therapy for refractory gastric cancer.

Results:



confirm



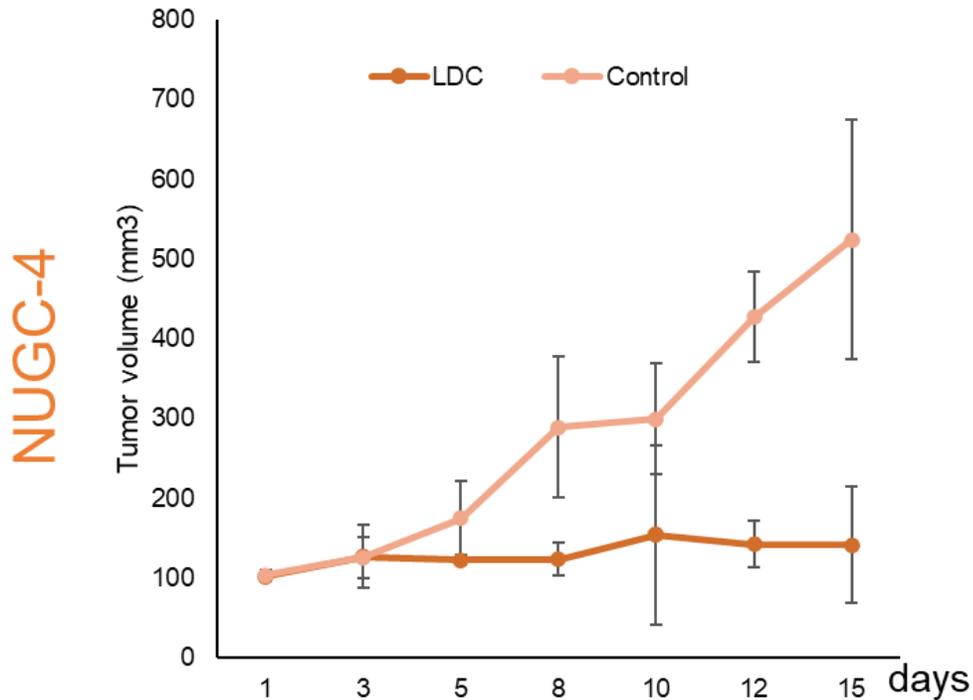
Yang Y, Akashi Y, Shimomura O, Tateno H, *et al*: Gastric Cancer 2022



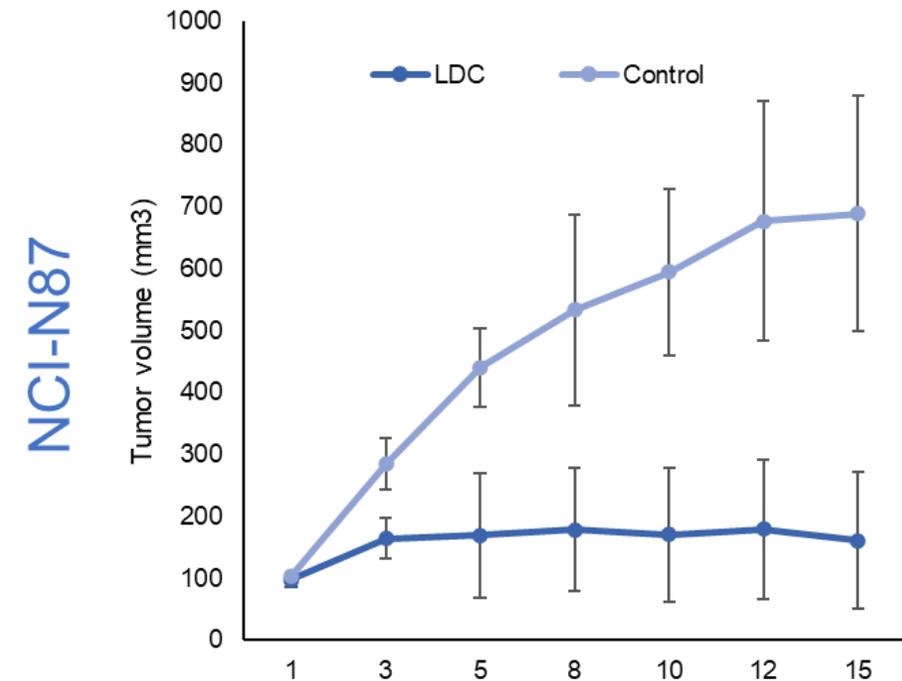


# LDC is also effective to stomach cancer models

## Scirrhou type



## Non-Scirrhou type



Yang Y, Akashi Y, Shimomura O, Tateno H, *et al*: Gastric Cancer 2022

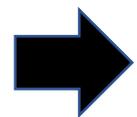


# Hemagglutination active is the biggest problem

Lectin was found as proteins cased **erythrocyte aggregation**. 1888 H. Stullmark



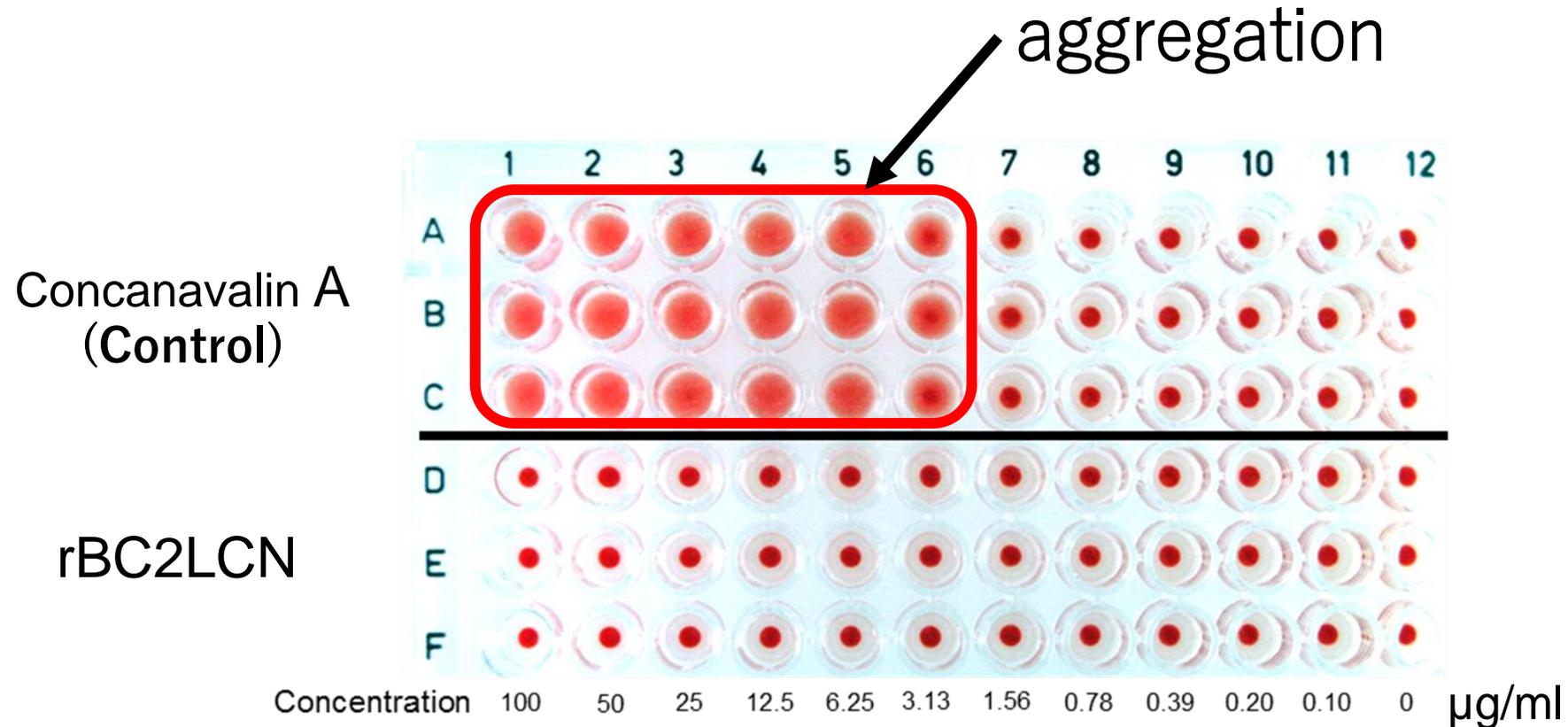
Posionous lectin; **Ricin (RCA1)** → **lethal dose 30 $\mu$ g/kg (human)**  
Olsnes S et al., Nature. 1974



**Generally, lectin is toxic to humans**



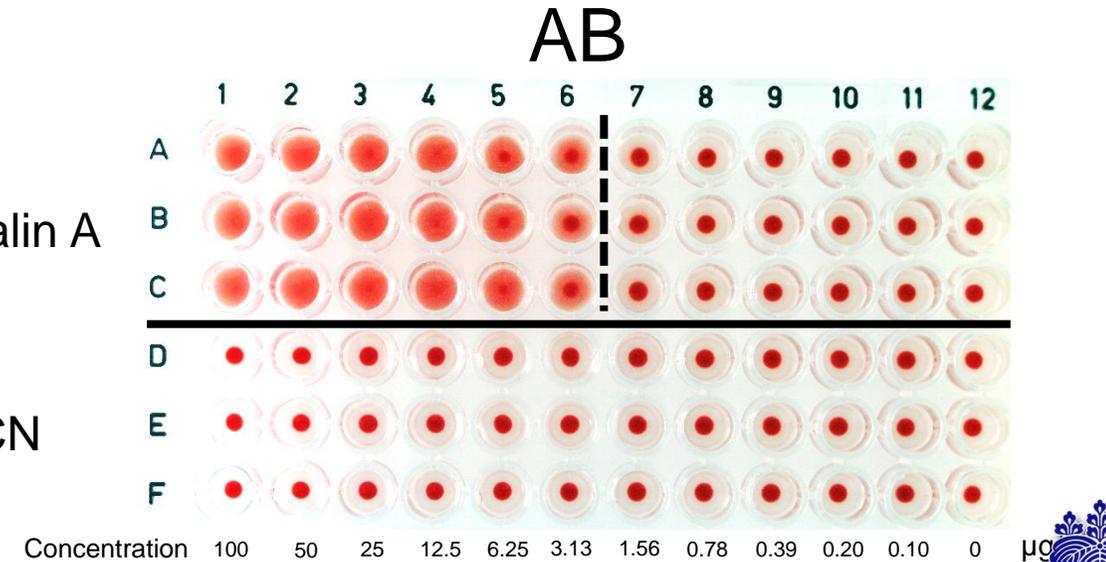
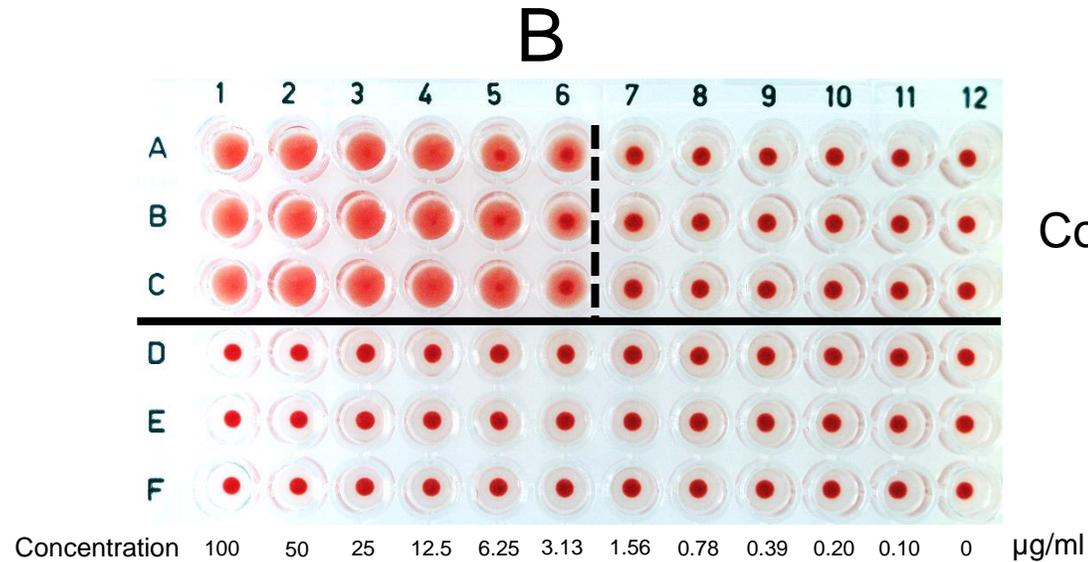
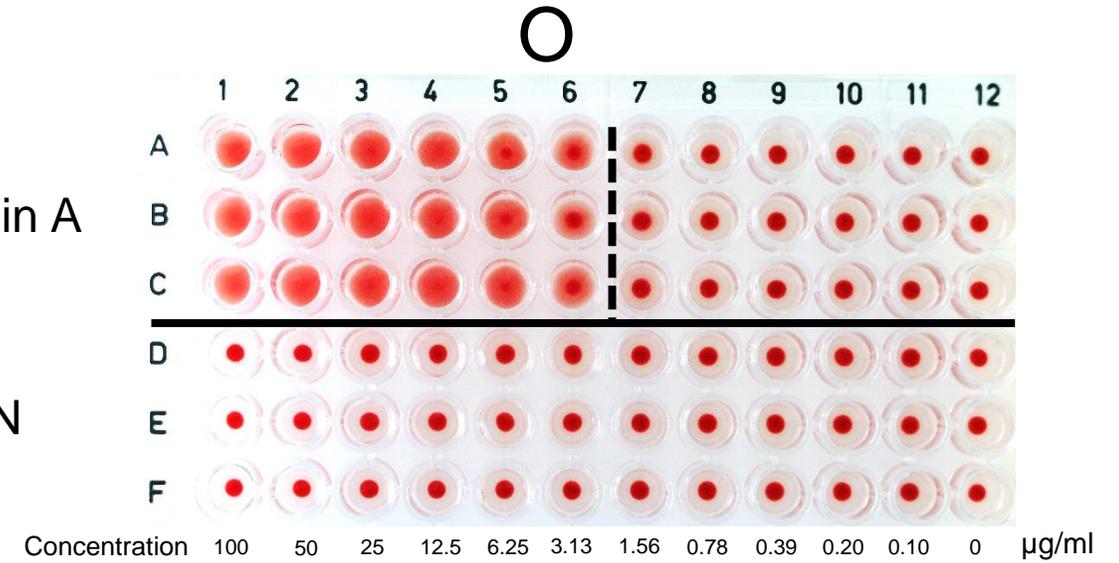
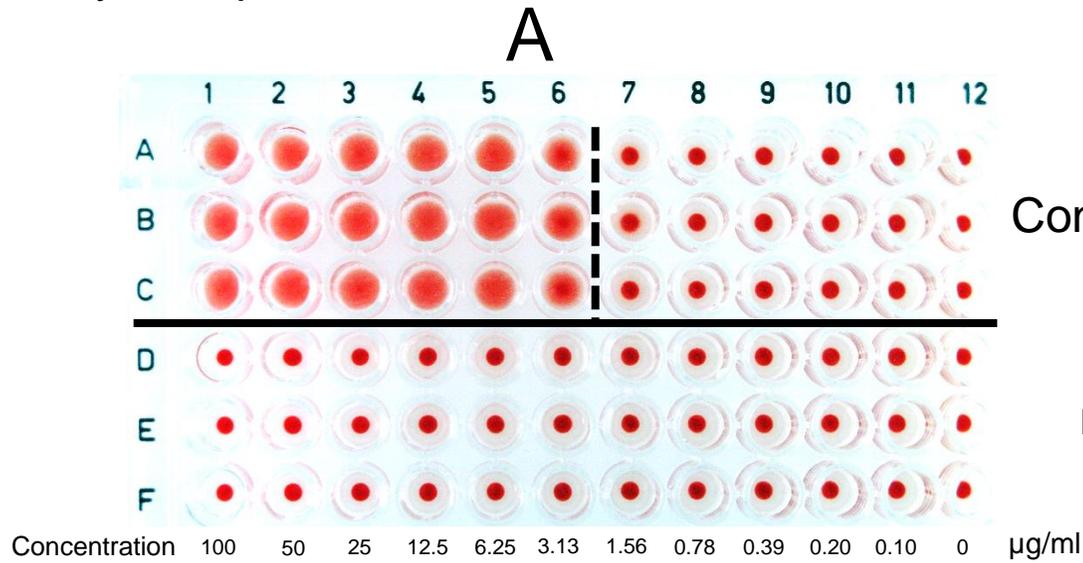
# rBC2LCN did not cause erythrocyte aggregation



Human Blood type A

# Hemagglutination test for human blood

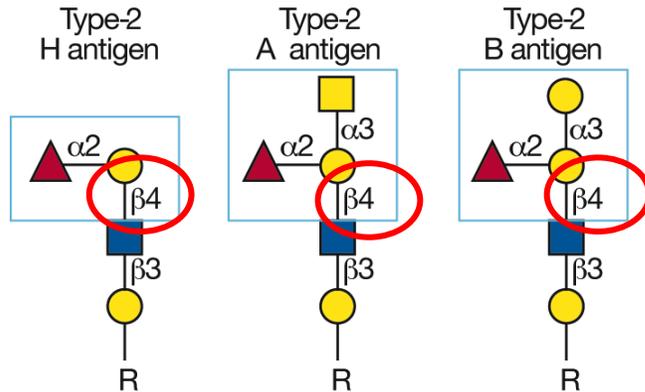
Sialydase process



# Blood type A,B,H determinants expressed by the epidermis are primarily constructed from type-2 units

Blood type

Type 2

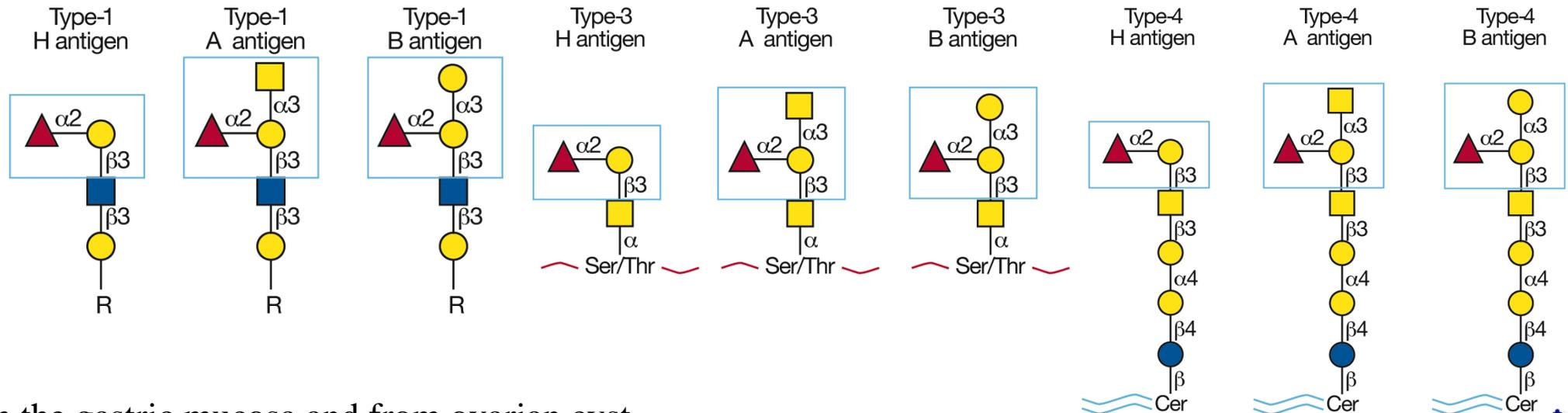


Essentials of Glycobiology

Second Edition

rBC2LCN recognize

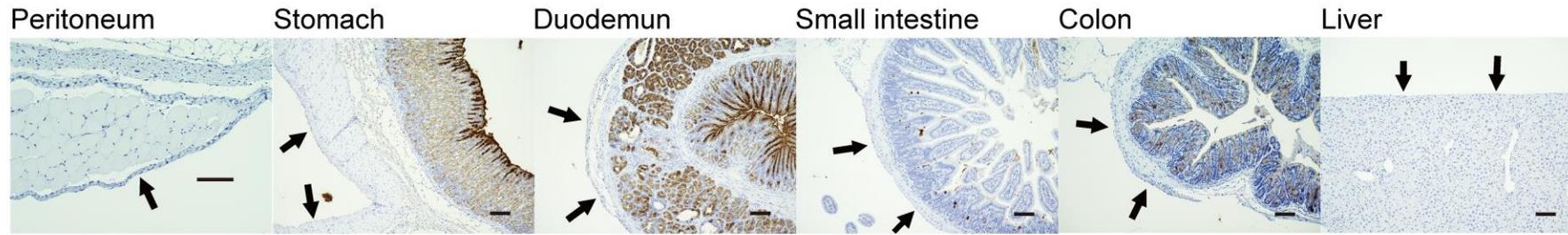
H Type 1/3/4



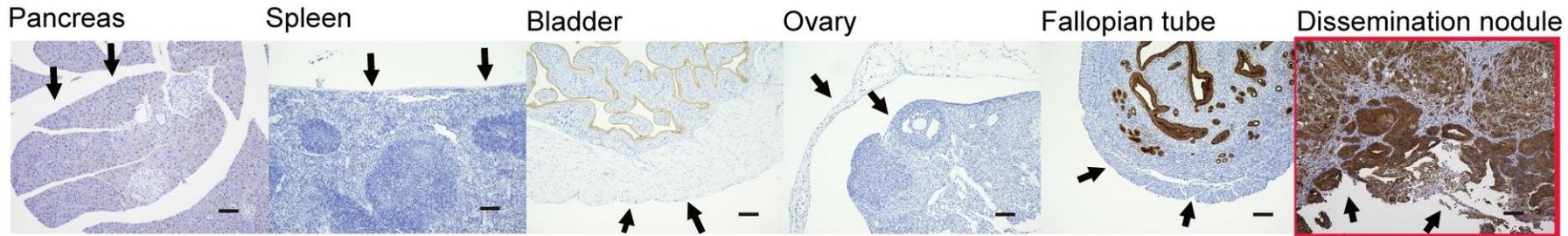
Mucins derived from the gastric mucosa and from ovarian cyst fluid express A, B, and H antigens on type-3 units



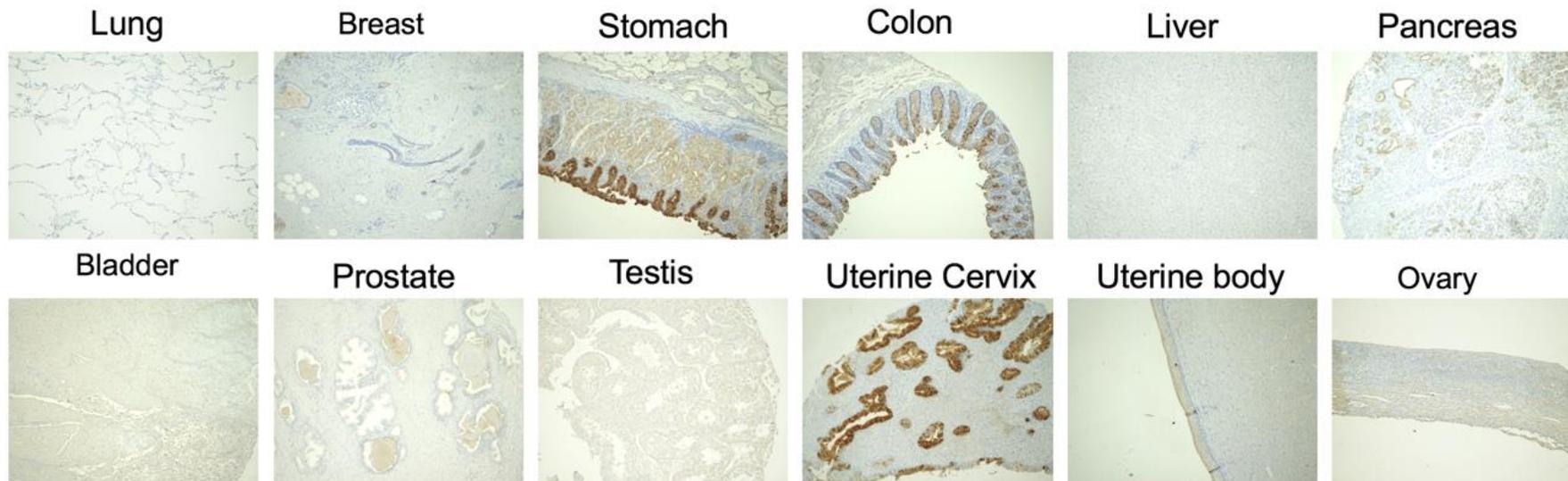
# rBC2LC-N Off site binding to human tissue



Mouse

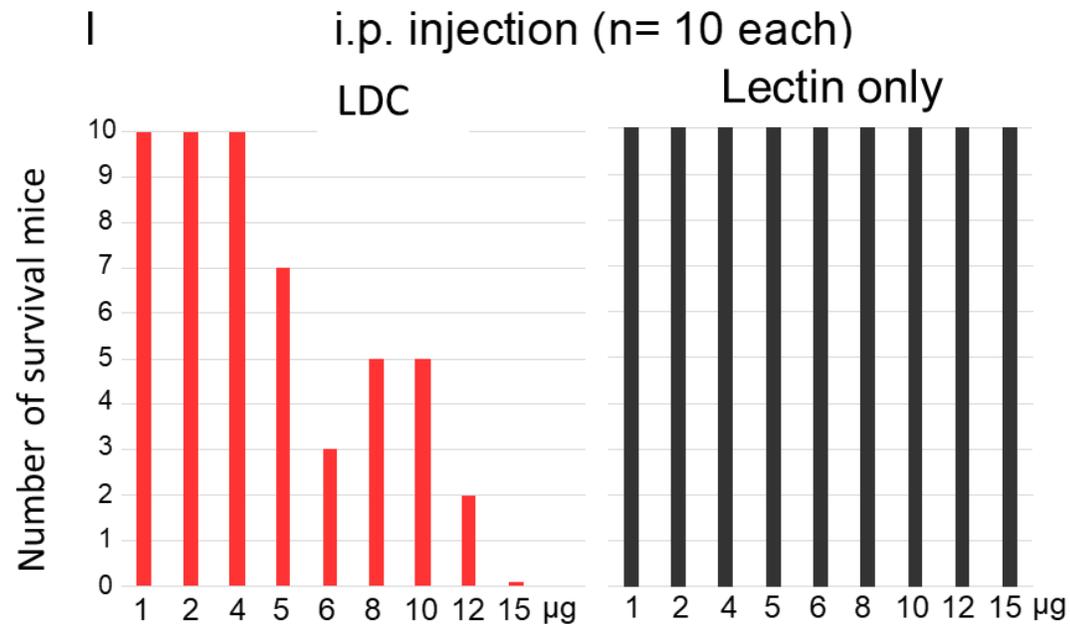


Human

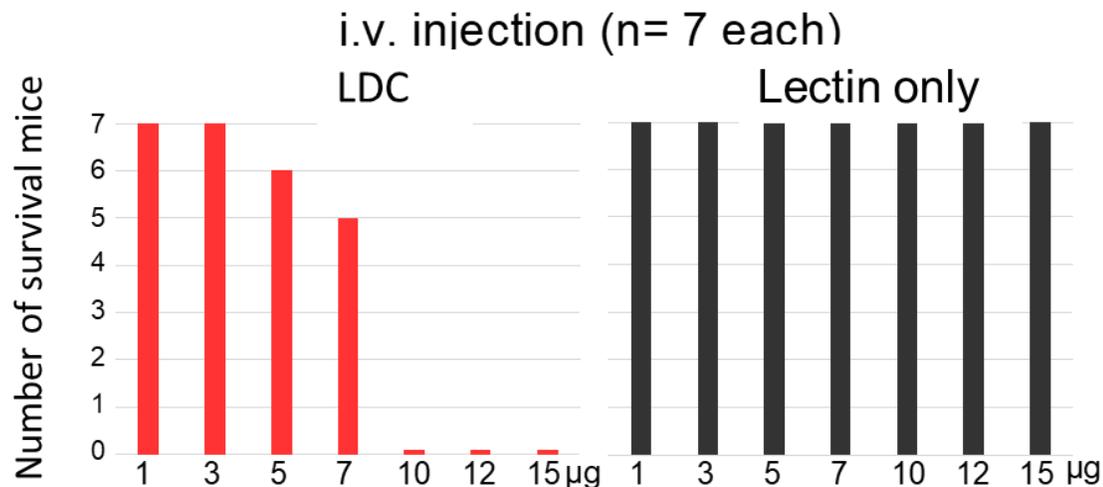


# Toxicity of LDC to wild mice

# LD50 test of LDC



LD50  $\doteq$  7μg/mouse



Lectin itself not toxicity up to 15 μg/mouse

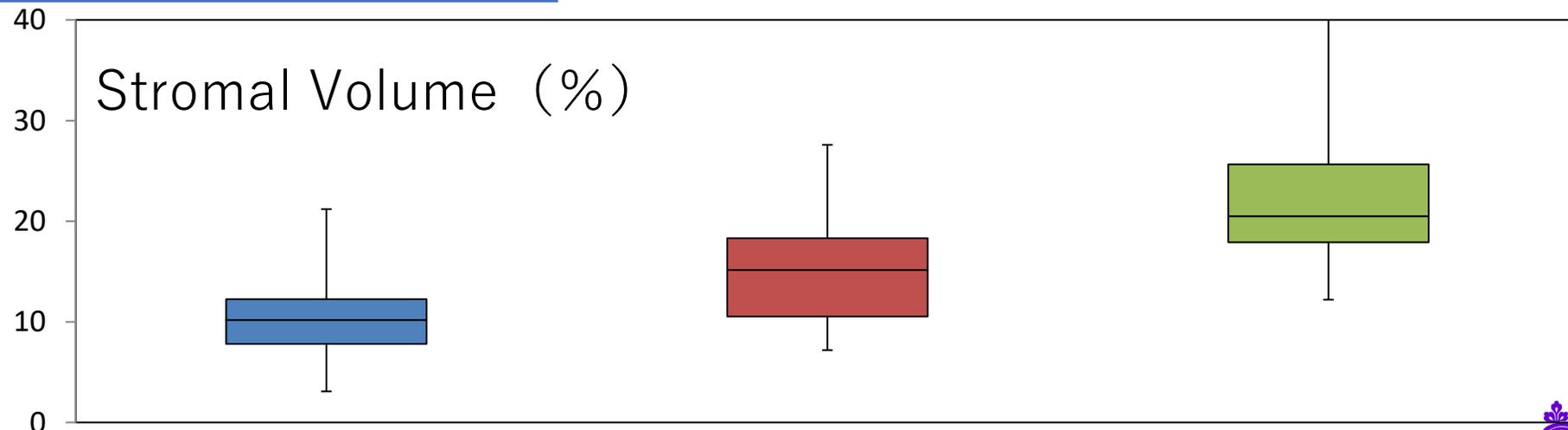
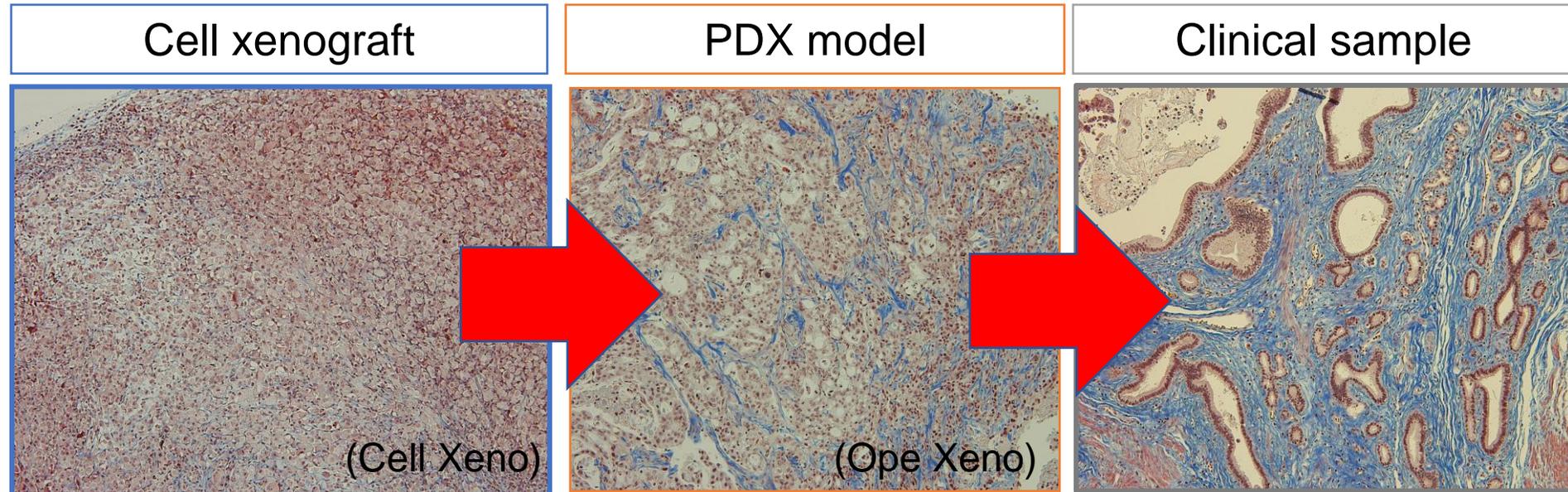


# Evaluation of LDC toxicity in large animals

- ✓ Liver, Kidney disorders were observed
- ✓ Lectin itself did not cause any side effects



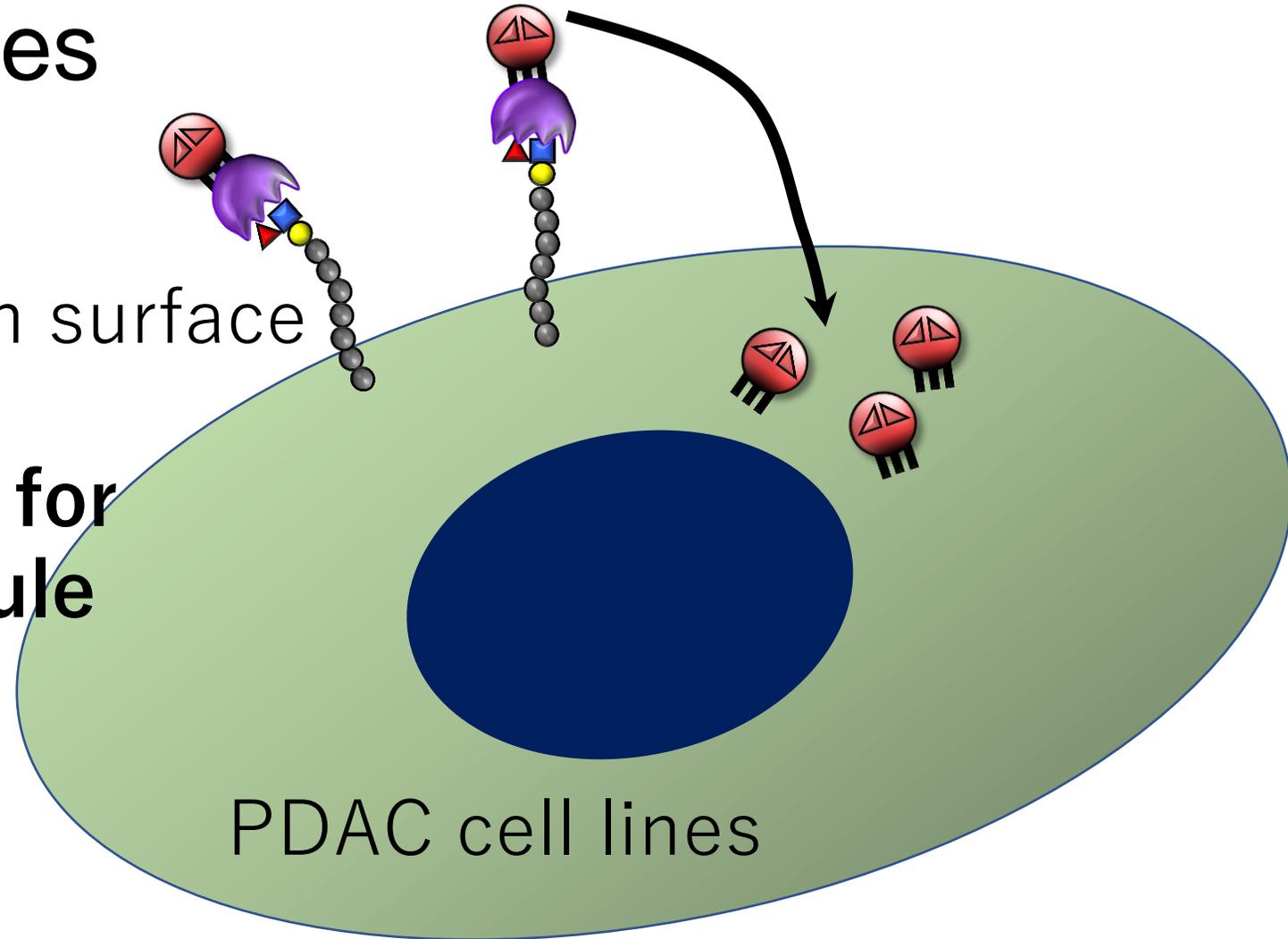
# Evaluate of LDC in closer to clinical sample



# Therapeutic experiments using pancreatic cancer cell lines

Glycans appear on surface

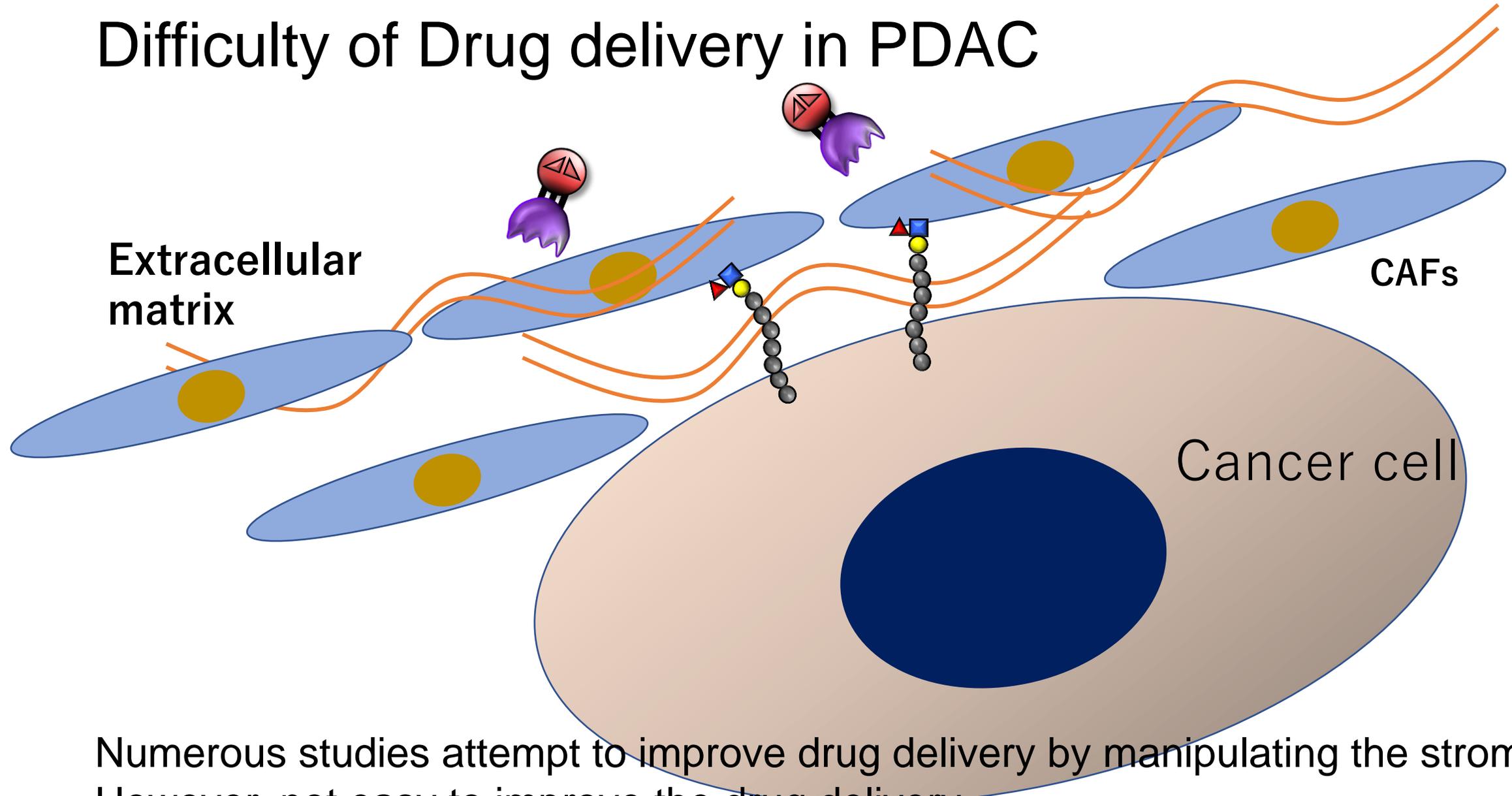
→ **easy to access for target the molecule**



PDAC cell lines



# Difficulty of Drug delivery in PDAC



Numerous studies attempt to improve drug delivery by manipulating the stroma. However, not easy to improve the drug delivery..

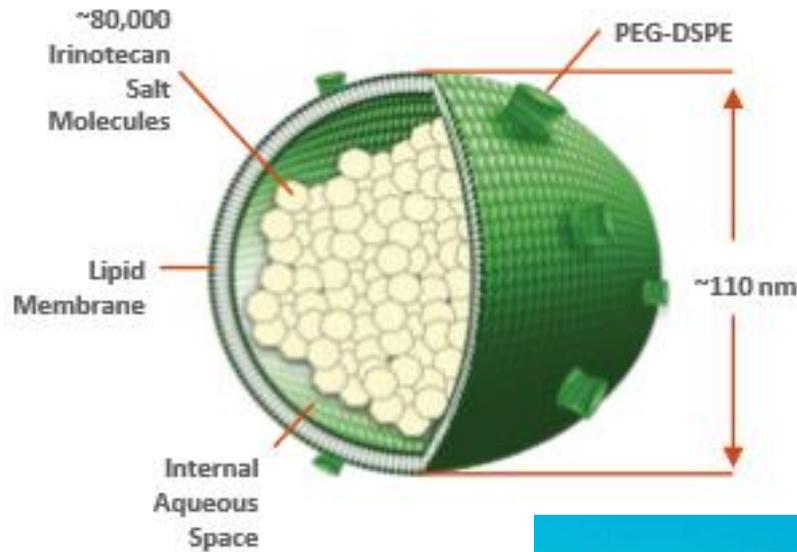


# For avoiding the BC2-PE38 side effects

- Application for liposomal drugs
- Photodynamic therapy

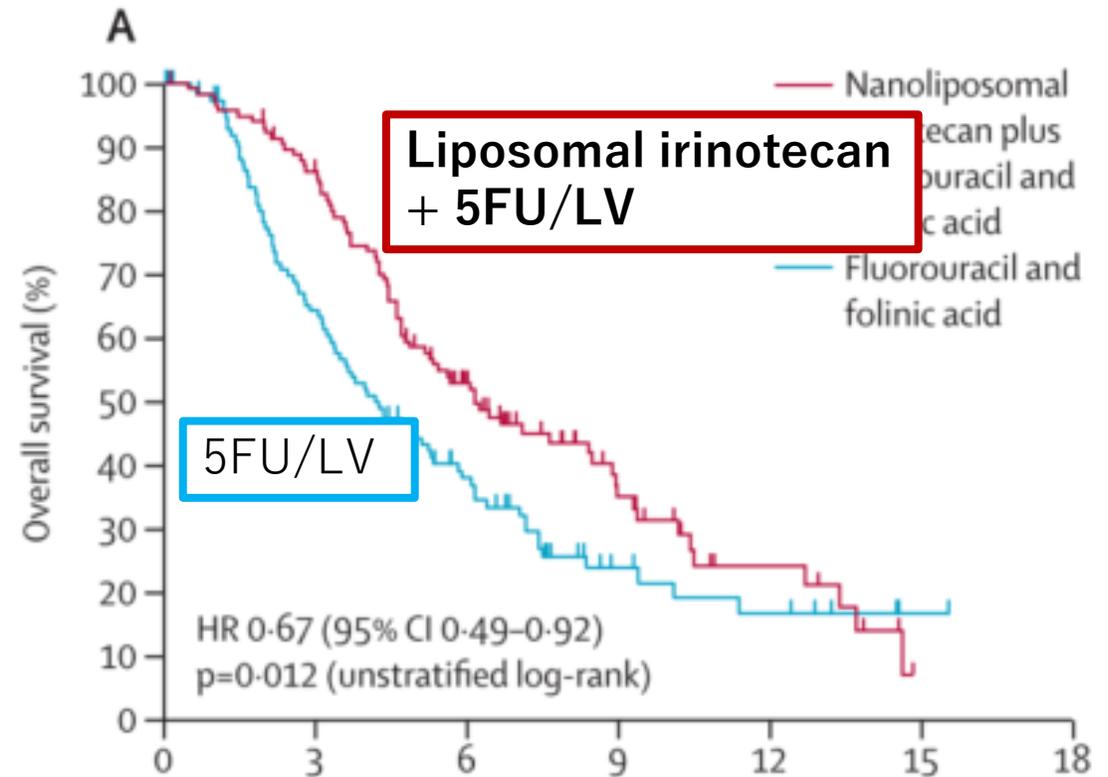


# Irinotecan liposome for pancreatic cancer patients



NAPOLI-1: a global, randomized, open-label, phase 3 trial.

Survival of Stage 4 PDAC patients

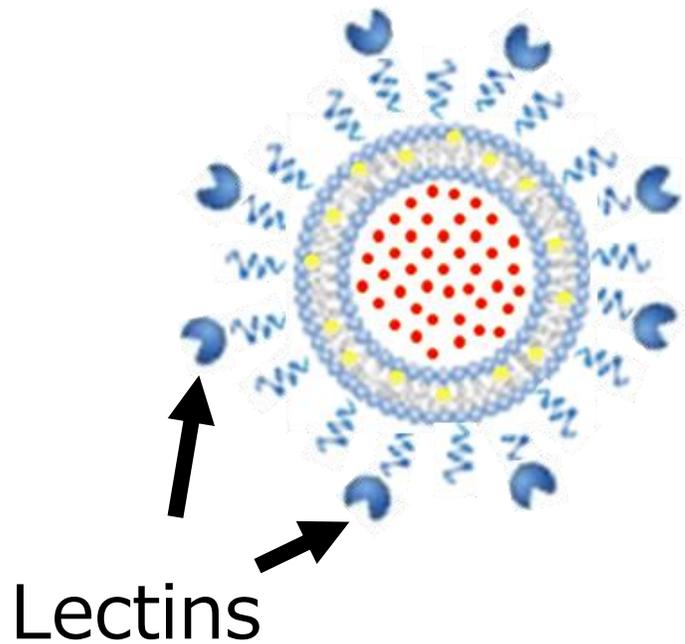


Wang-Gillam A, et al. Lancet. 2016;387(10018):545-57



# Active Targeting by lectin coating liposome drugs

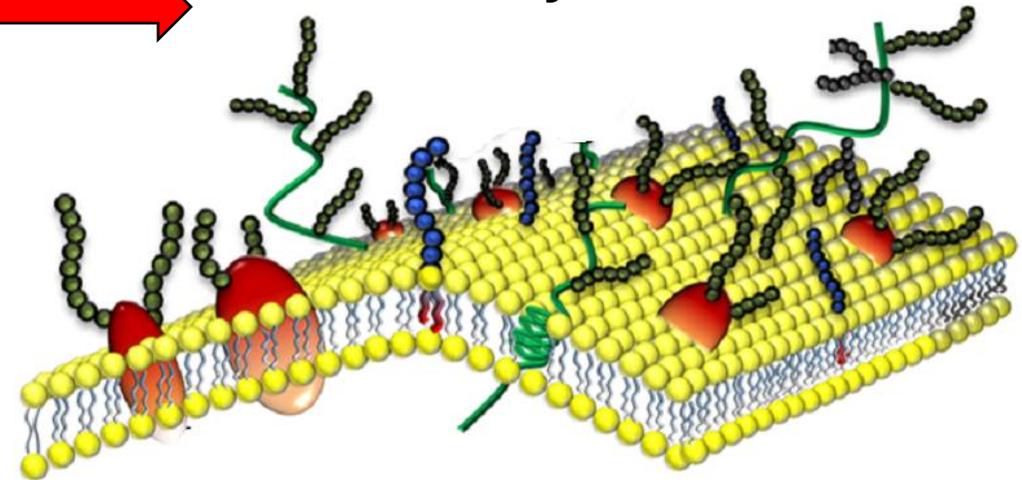
## Lectin coating liposome



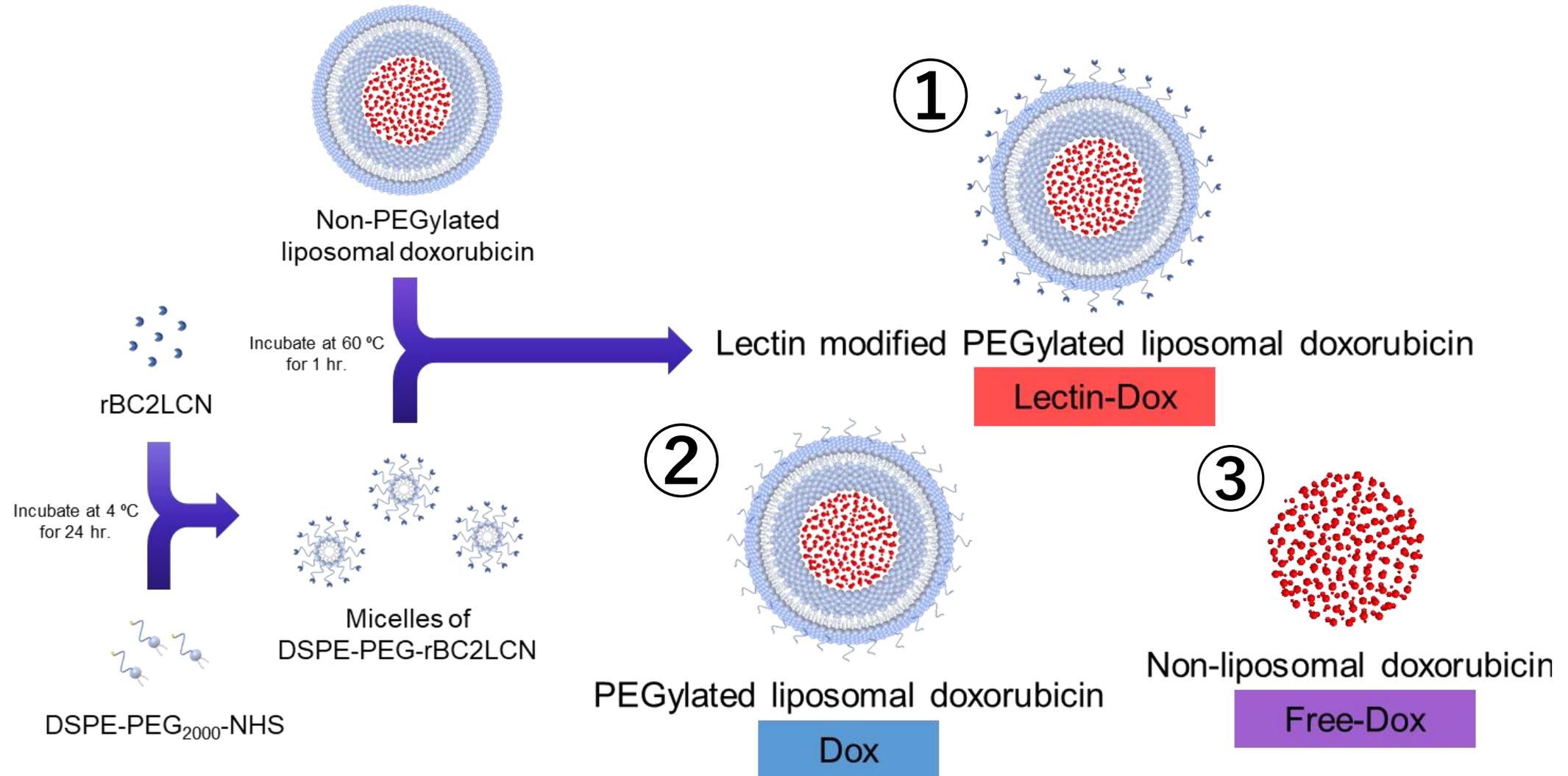
*Active Targeting*



**Cancer-Glycan**



# Preparation of lectin coating liposome

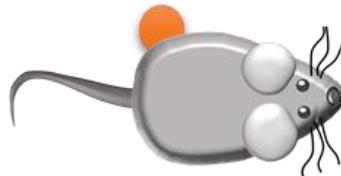


# Treatment with lectin coating liposome drugs

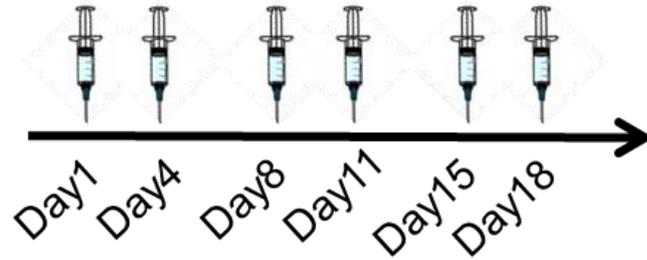
Capan-1/SUIT-2  $2 \times 10^6$  /mouse  
subcutaneous injection



14 days



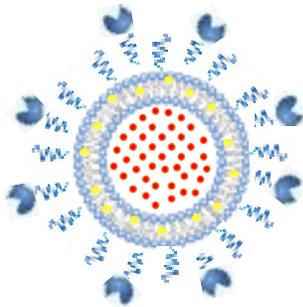
Intravenous injection twice per week  $\times$  3 weeks  
(doxorubicin concentration 2 mg/kg)



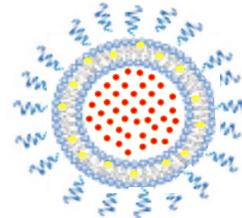
Sacrificed at Day 22

BALB/c nude mouse ♀ 7-8w

① lectin coating liposome



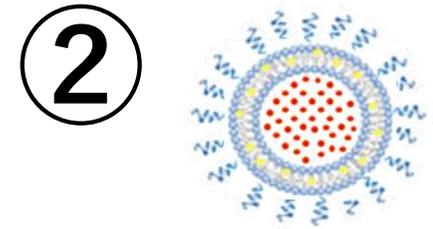
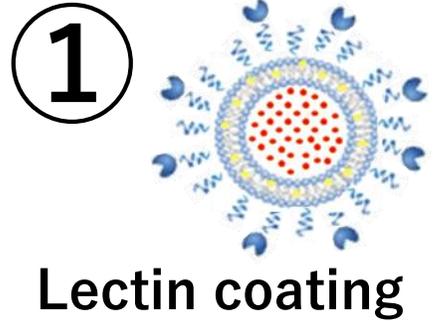
② non-coating liposome



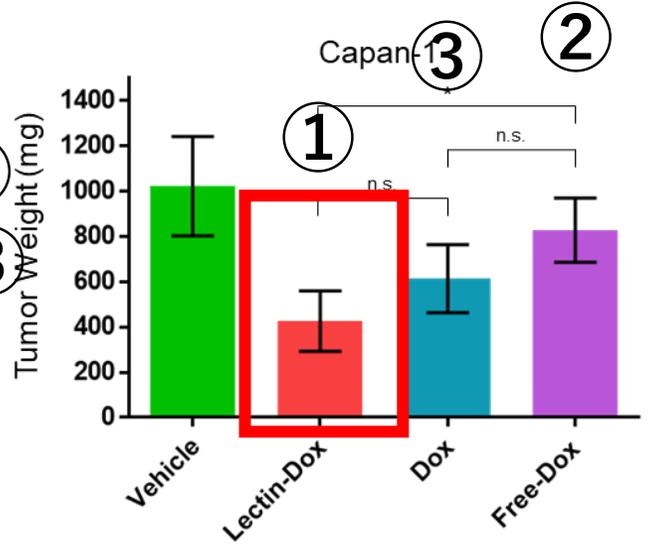
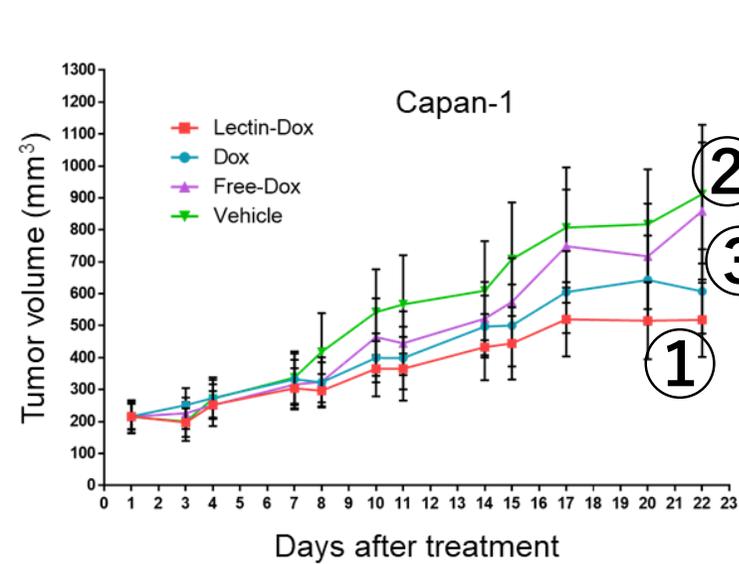
③ Free Dox



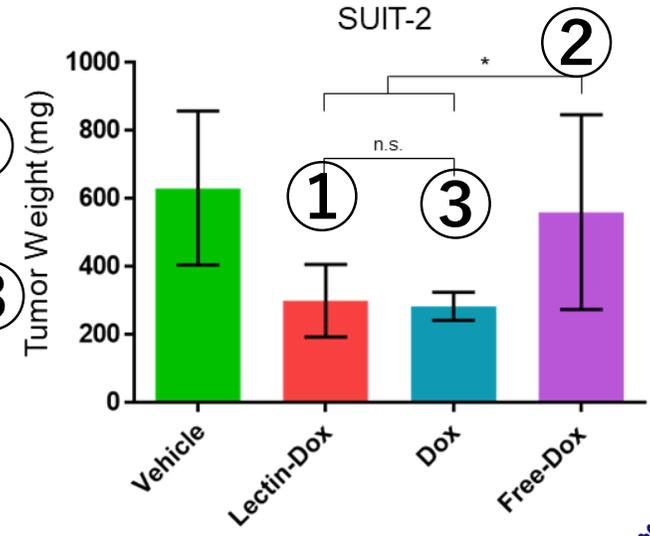
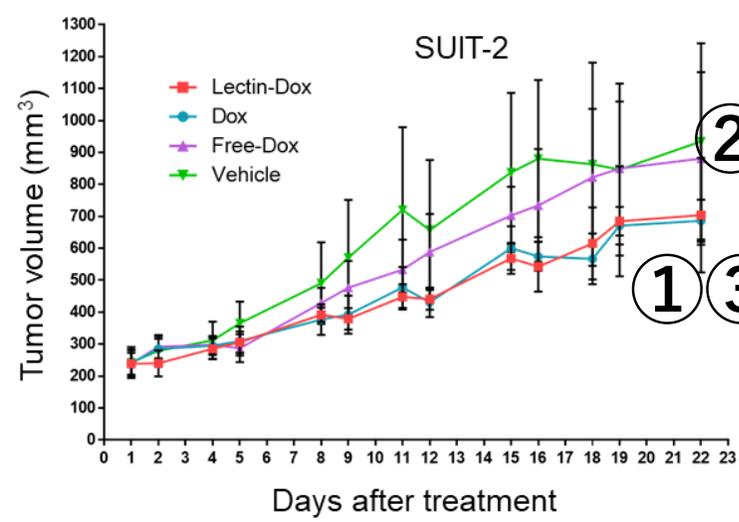
# DDS improve by lectin coating liposome



**Capan-1**

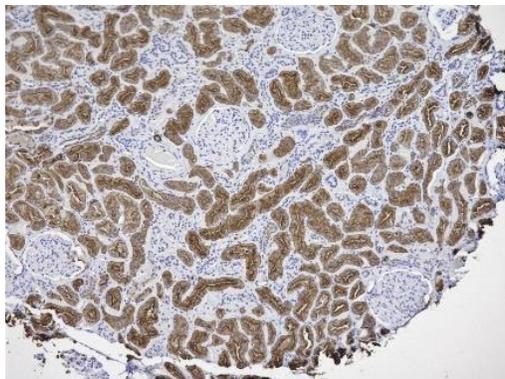
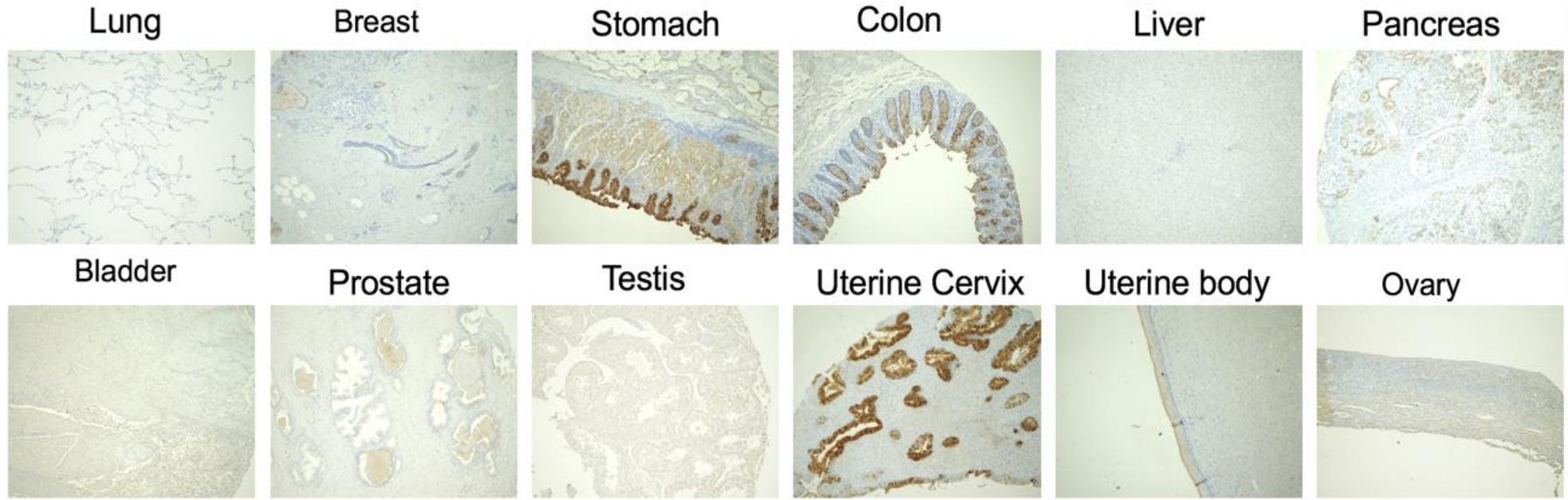


**SUIT-2**



# Off site binding of rBC2LCN lectin

Human  
organs



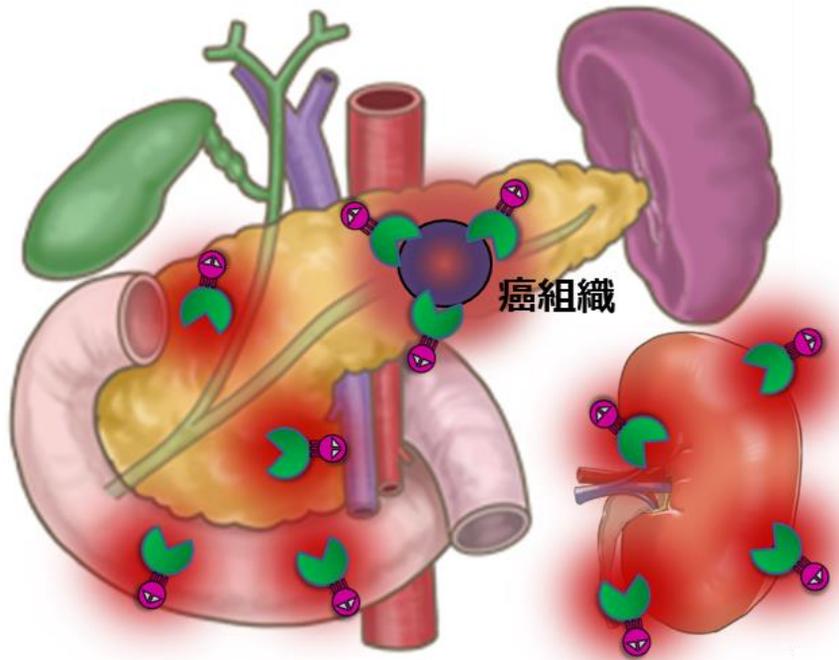
**Kidney**

Systemic administration may  
cause adverse events

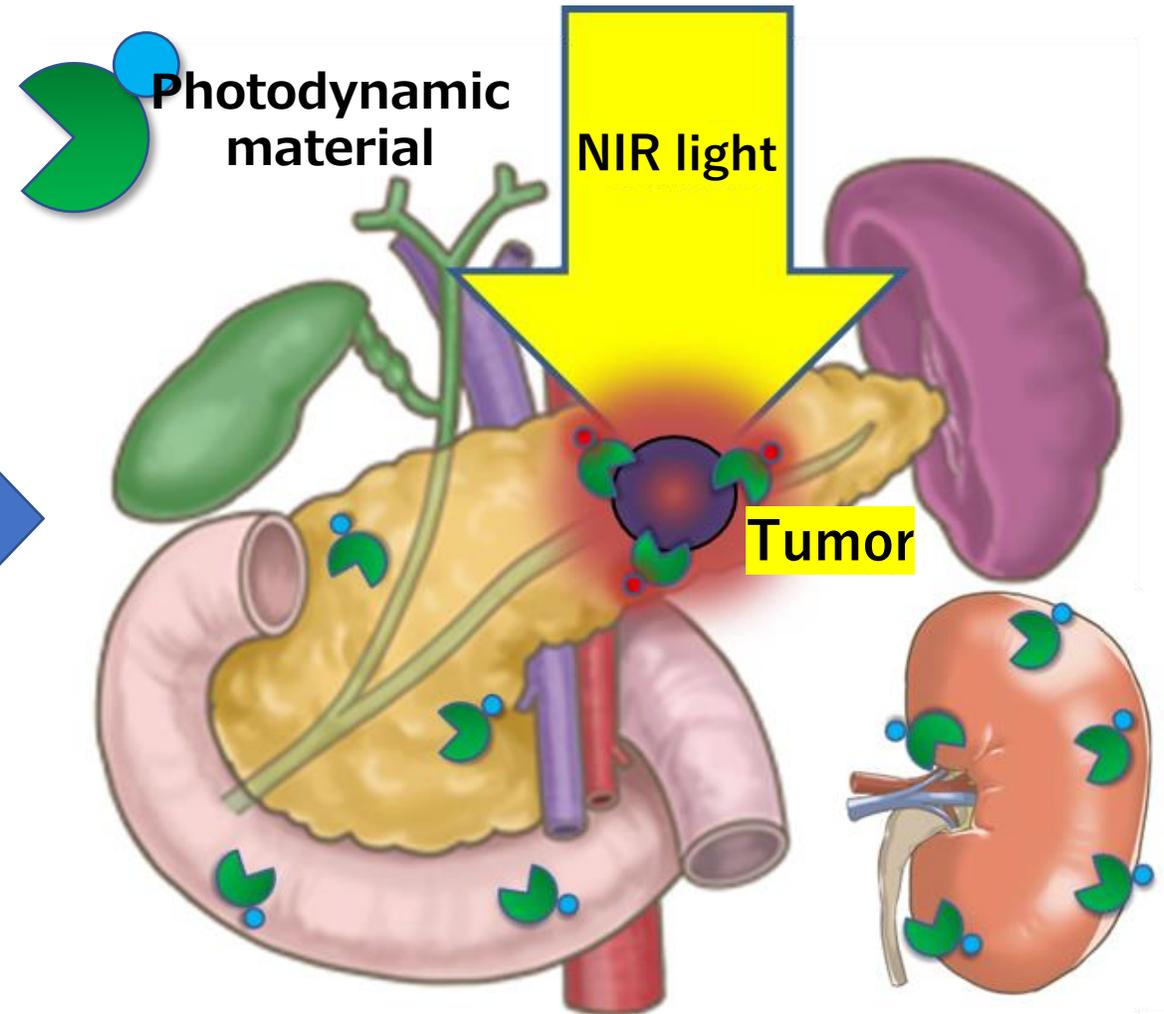
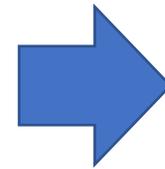


# Reducing the off site effect on LDC injection → fuse with Photodynamic therapy

Systemic injection of LDC

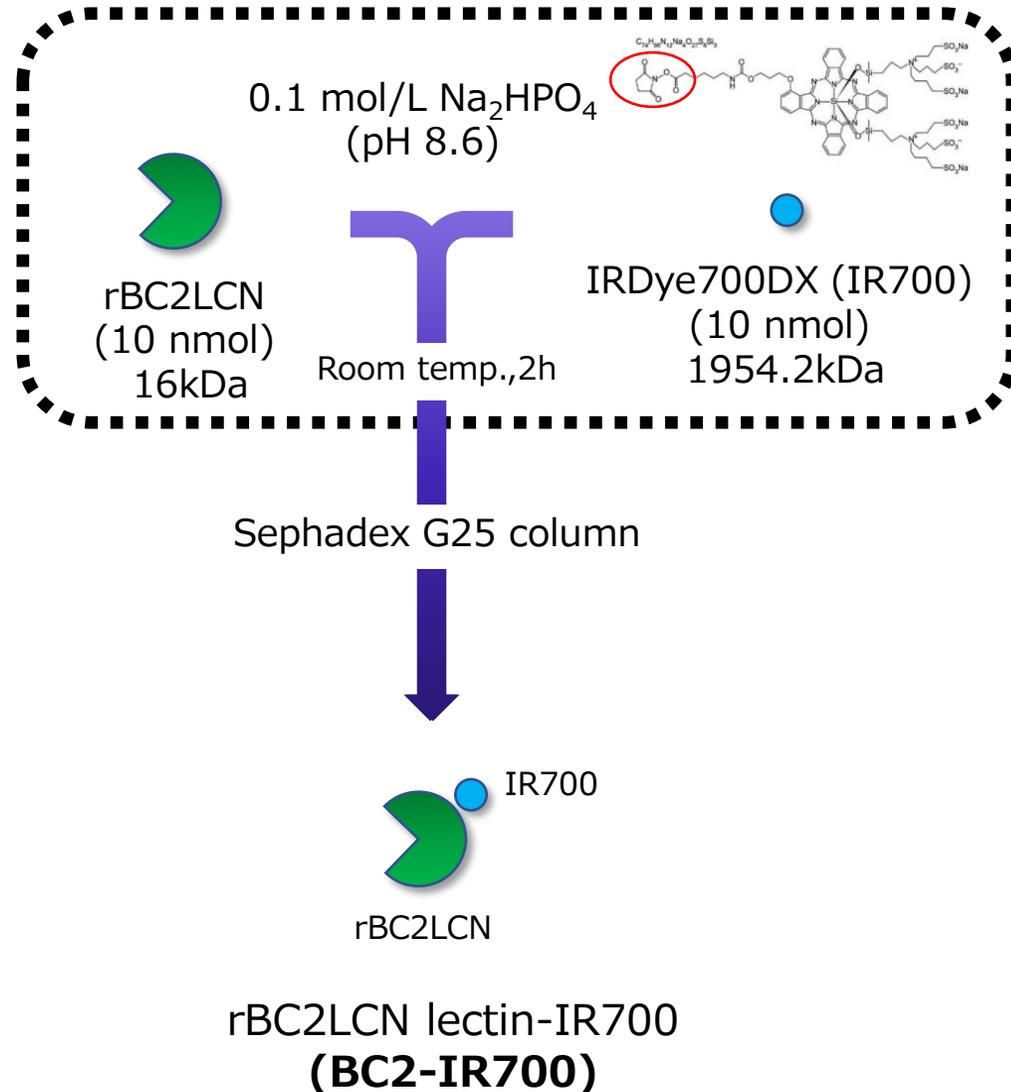


Side effect to normal organs

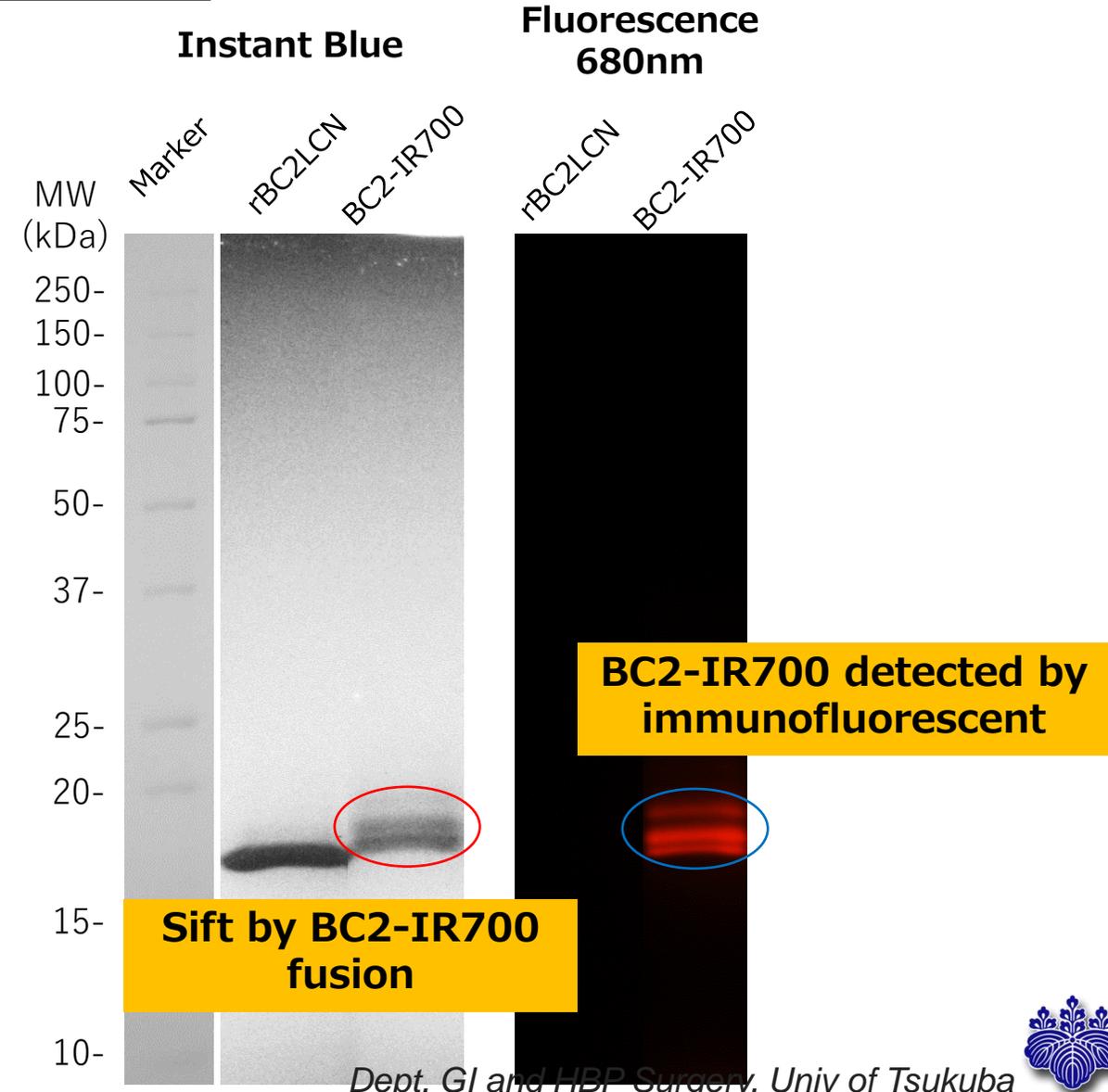


# Preparation of rBC2LCN lectin-IR700

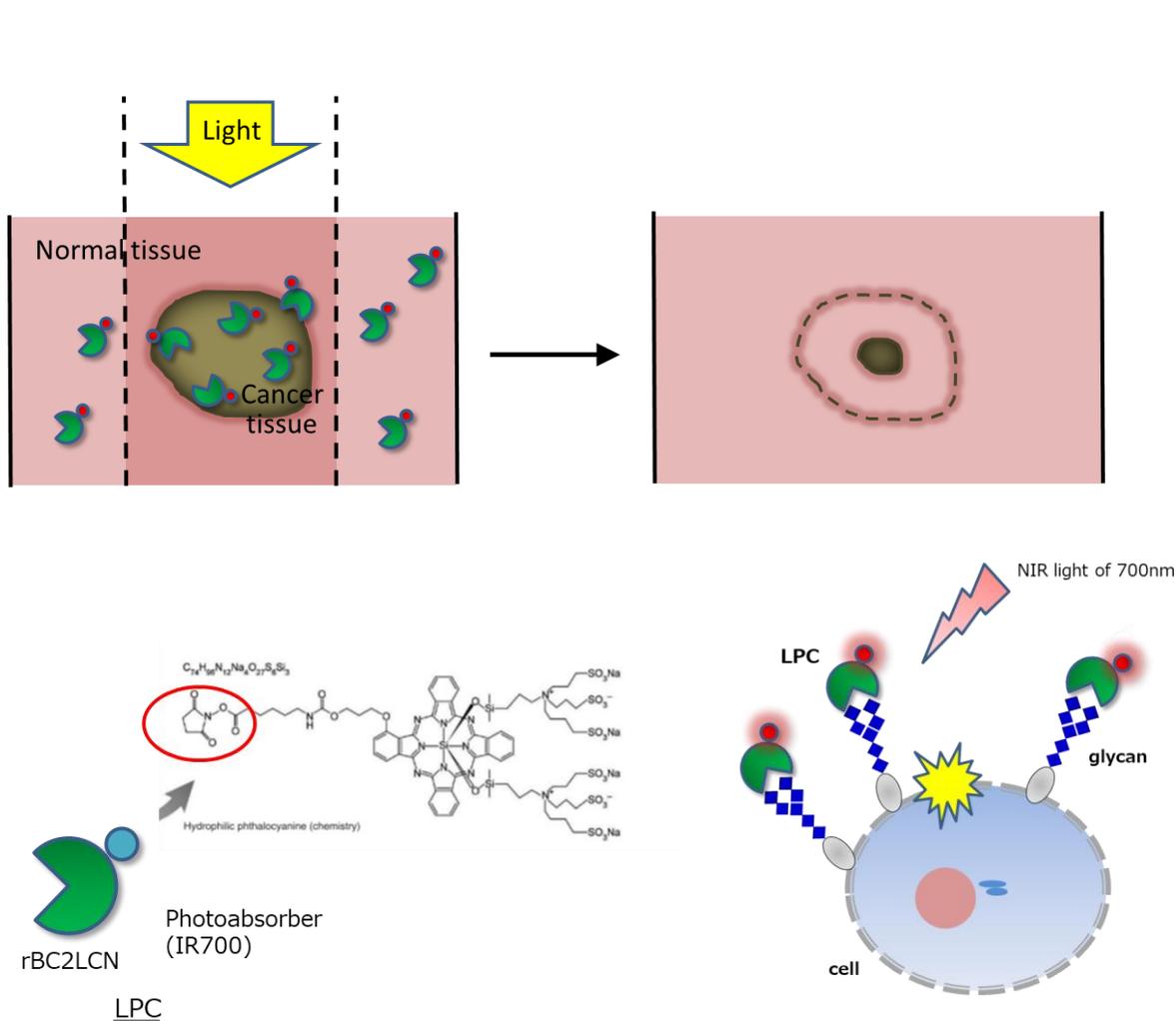
Kuroda, Shimomura, Tateno et al., Int J Cancer. 2022



## SDS-PAGE



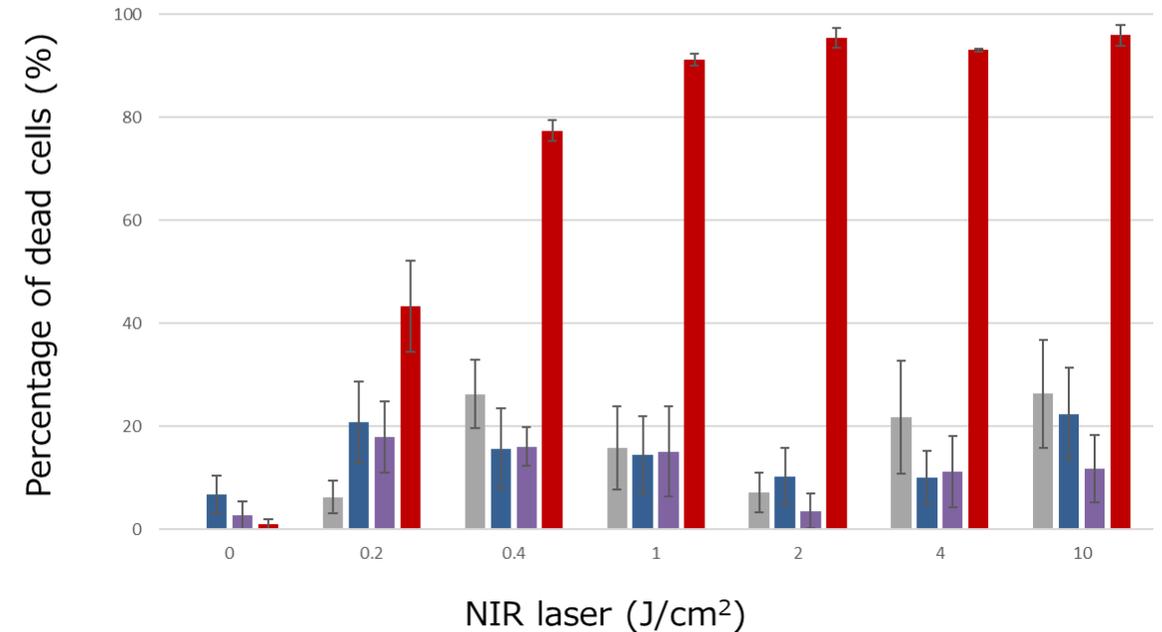
# Pancreatic cancer cell line Tx by rBC2-IR700



*in vitro* NIR phototherapy



**Capan-1**

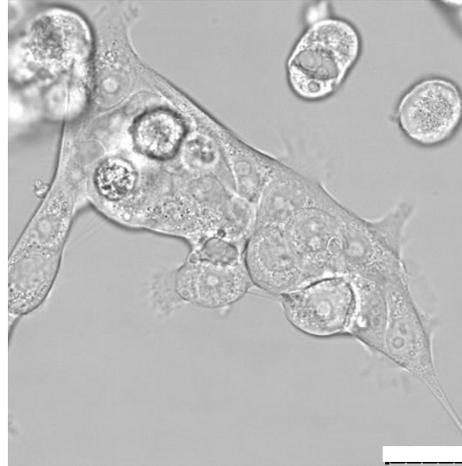


# Evaluate the binding ability

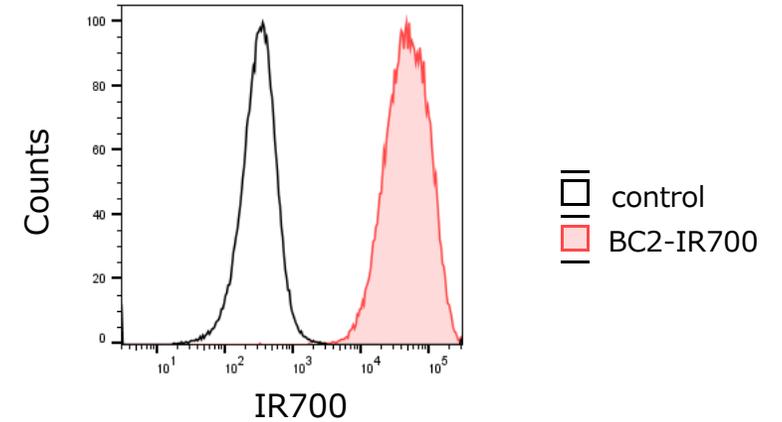
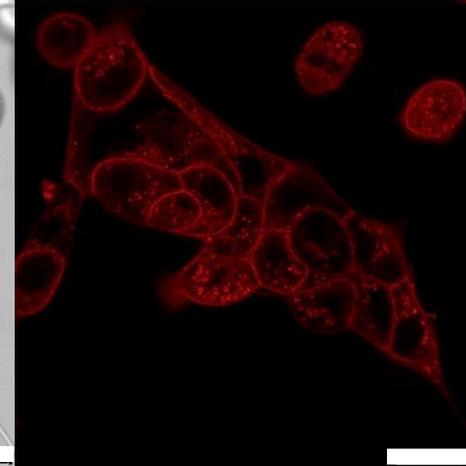
Kuroda, Shimomura, Tateno et al., Int J Cancer. 2022

**Capan-1**  
**(target glycan +)**

**Phase contrast**

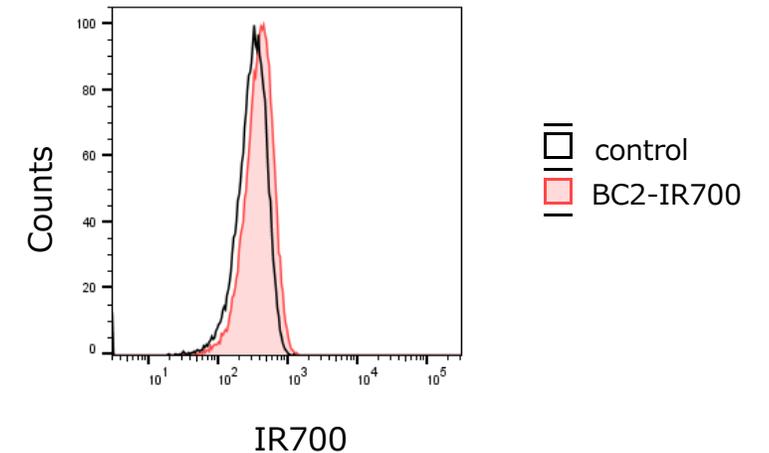
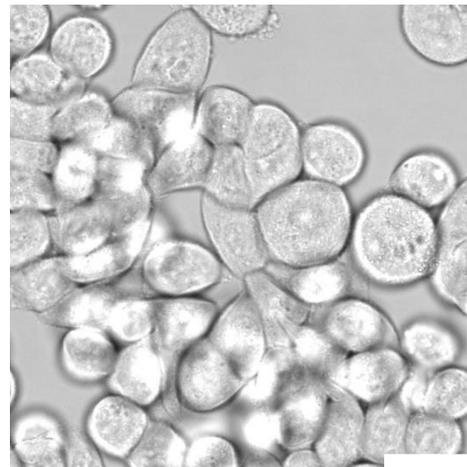


**IR700**



**Specific binding to glycans**

**SUIT-2**  
**(target glycan-)**



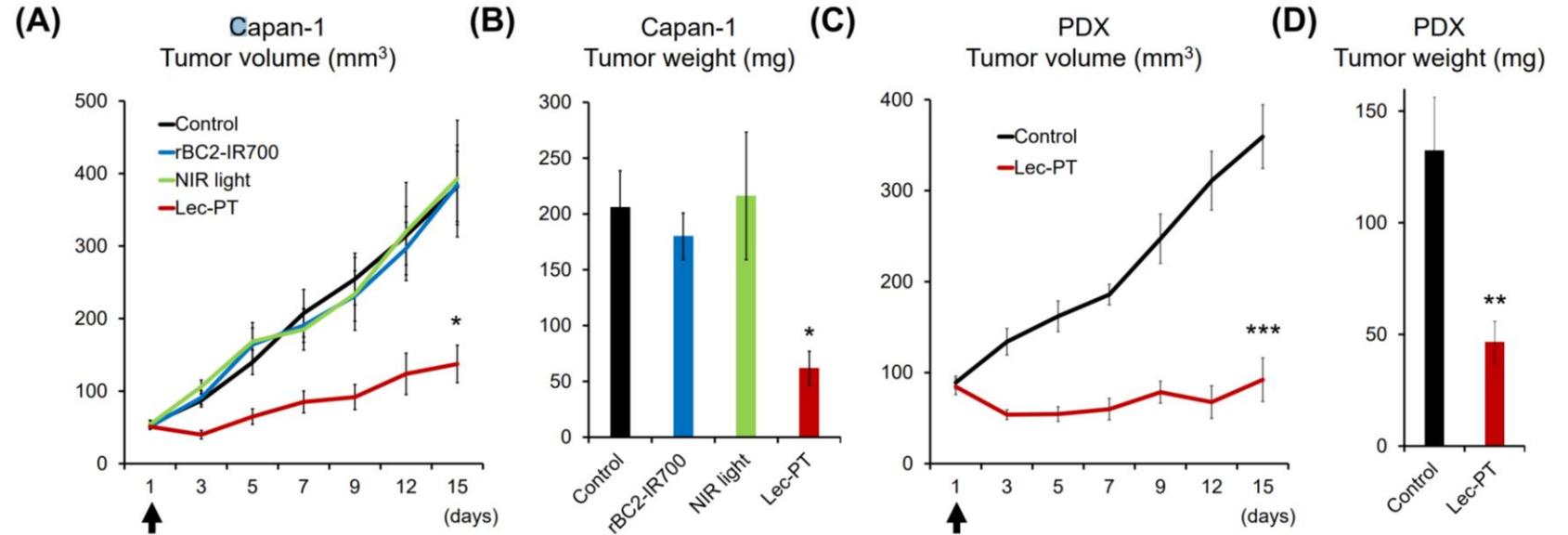
Scale bars = 25 $\mu$ m

Dept. GI and HBP Surgery, Univ of Tsukuba

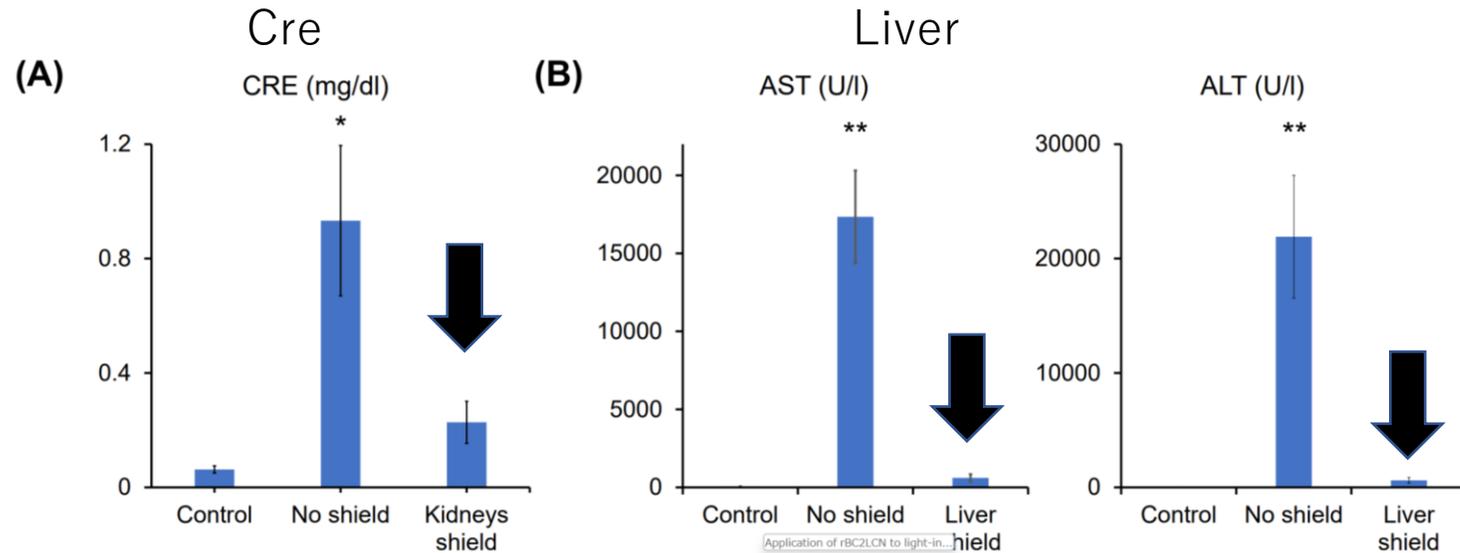


# BC2-IR700

Injection + NIR light  
(Capan-1 xeno)



Protecting NIR light



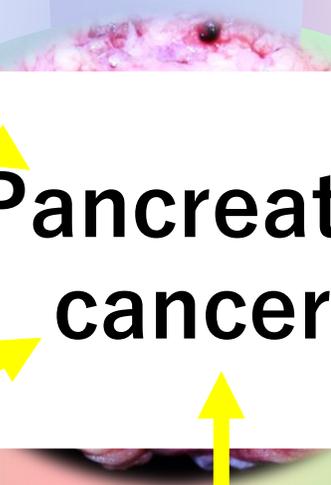
# Ongoing project for pancreatic cancer research

## Stromal CAFs

## Oncogene

KRAS inhibitor  
cfDNA, ctDNA, miRNA

Stroma penetrating peptide  
Anti-stromal antibody



**Pancreatic  
cancer**

## Cancer immunity

Anti-PD 1 antibody  
Immunotherapy

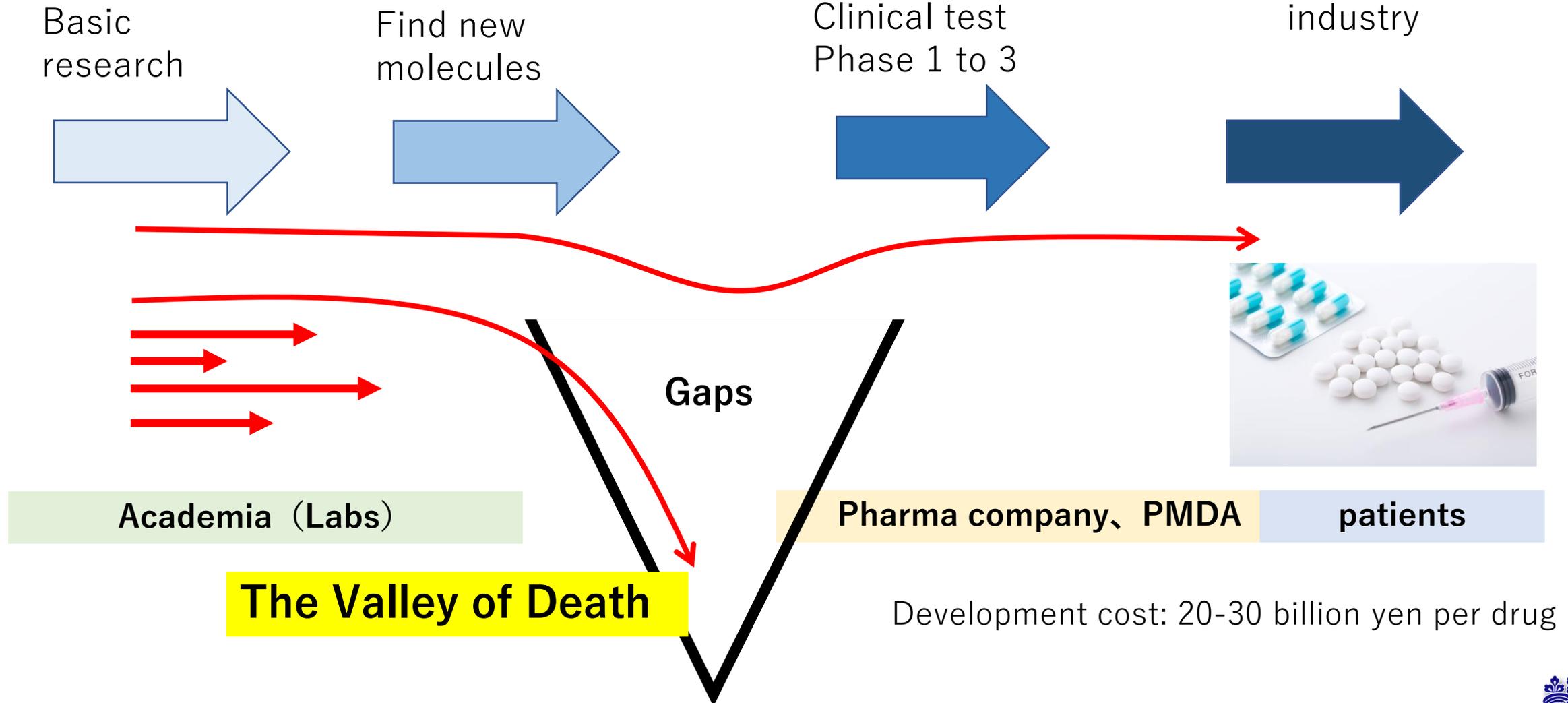
## Glycan

Glycan target therapy  
Tumor biomarker

## Drug resistance

# Goal of basic research

→ develop therapeutic & diagnostic methods



# Take Home Message

- Early detection is only way for cure from pancreatic cancer
- Lectin-drugs conjugate (LDC) have high therapeutic efficacy, but there are still hurdles to overcome in their application to clinical pancreatic cancer
- Collaborate Efforts Needed to Improve Pancreatic Cancer Prognosis

