

外科的同所移植マウスを用いる  
抗がん剤の薬効評価、受託サービス  
Services of Efficacy Testing of AntiCancer  
Drug by SOI mouse model



AntiCancer Japan Inc.

Tatushi Goto

May 8<sup>th</sup>, 2013 Biotech2013

# AntiCancer Japan Inc.

## Business

### Product sales

- GFP/RFP-expressing cell lines (Wako Pure Chemical Industries Ltd.)
- GFP-expressing nude mouse (Japan SLC Inc.)

### Contract research using *in vivo* fluorescent imaging technology

- Tumor imaging (SOI model, SC model, TVI model)
- Drug distribution

### Demonstration

## Location

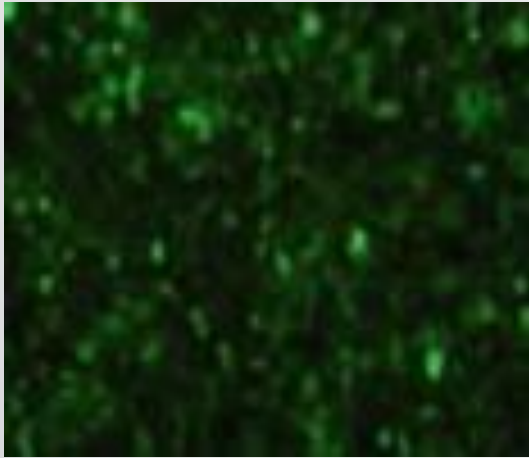
〒567-0085

Saito Bioincubator 106, 7-7-15 Saitoasagi, Ibaraki, Osaka

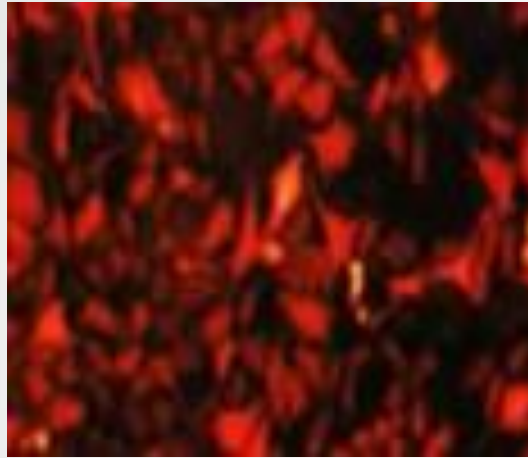
URL: <http://www.anticancerjapan.com/>



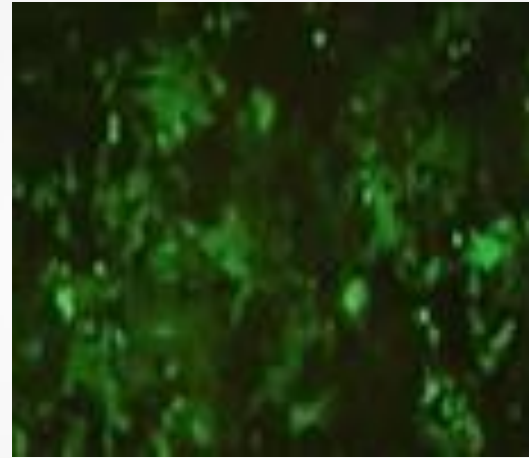
# GFP/RFP-expressing cell lines



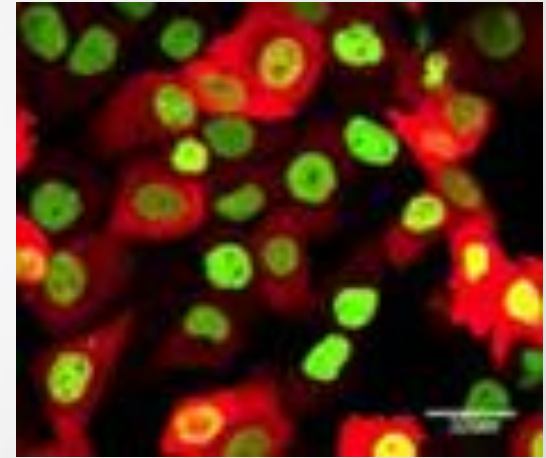
PC3-GFP



PC3-RFP



HCT116-GFP



HT1080-Dual color

**Now on sale !!**

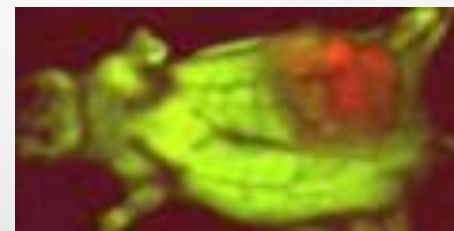
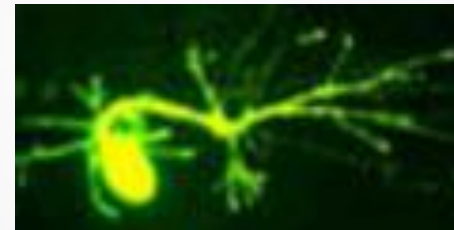
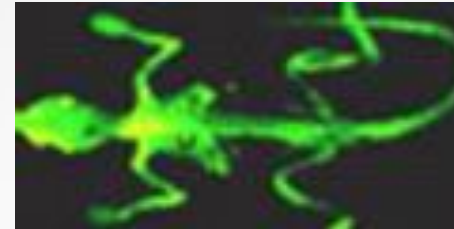
**Wako Pure Chemical Industries**

<http://www.wako-chem.co.jp/siyaku/product/life/anti/index.htm>

**AntiCancer Japan**

[http://anticancerjapan.com/research/fluorescent\\_protein/index.html](http://anticancerjapan.com/research/fluorescent_protein/index.html)

# GFP-expressing nude mouse



RFP nude mouse



CFP nude mouse



**Japan SLC**

<http://jslc.co.jp/>

**AntiCancer Japan**

[http://anticancerjapan.com/research/mousenude\\_protein/index.html](http://anticancerjapan.com/research/mousenude_protein/index.html)

“Implantation of human tumor tissue into the corresponding organ of mouse ”

# SOI model

**SOI** = Surgical Orthotopic Implantation

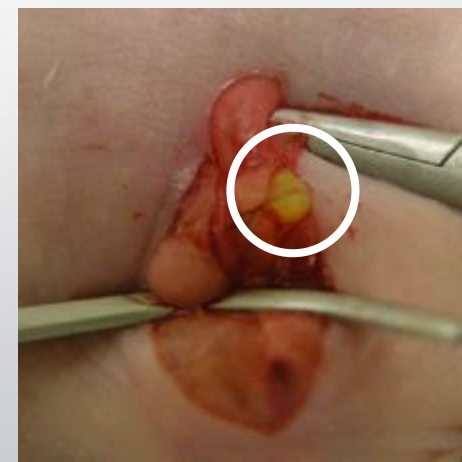
Prostate cancer Cell line: PC3-GFP



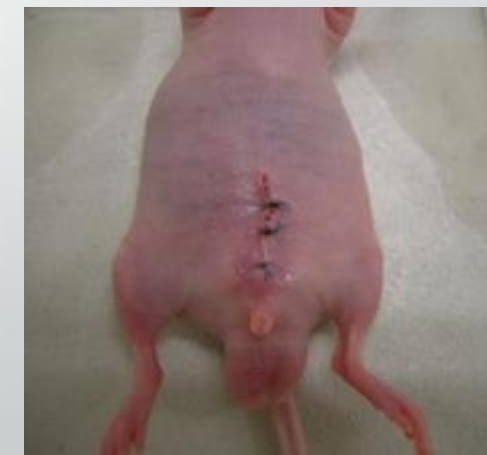
① Cut subcutaneous tumor into small pieces.



② Expose prostate.



③ Implant on prostate using nylon suture.



④ Close a wound.

“Implantation of human tumor tissue into the corresponding organ of mouse”

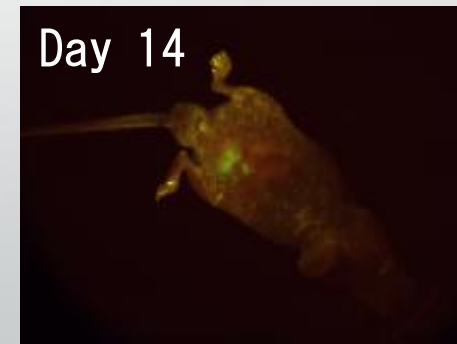
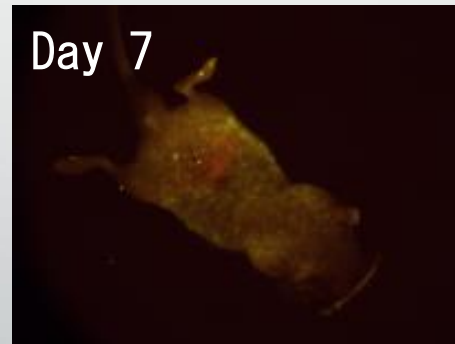
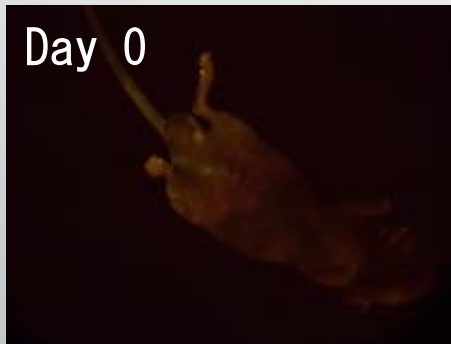
## SOI model

Prostate cancer Cell line: PC3-GFP

SC



SOI



**SOI** model mouse shows tumor metastasis.



“Implantation of human tumor tissue into the corresponding organ of mouse ”

## SOI model

Breast cancer	No. of mice	No. of mice with Primary tumor	No. of mice with lung metastasis
SOI	8	8	6
SC	7	7	0

(Fu *et al*, *Anticancer Res.*, 1993)

Colon cancer	Local tumor growth	Metastasis			
		Regional lymph node	Peritoneum	Liver	Lung
SOI	12 / 12	6 / 12	10 / 12	9 / 12	6 / 12
Cell suspension	3 / 12	0 / 12	0 / 12	0 / 12	0 / 12

(Furukawa *et al*, *Jpn J. Surgery.*, 1993)

**SOI model enhances metastatic ability of tumor.**

“Implantation of human tumor tissue into the corresponding organ of mouse ”

## SOI model

Ovary



Stomach



Colon



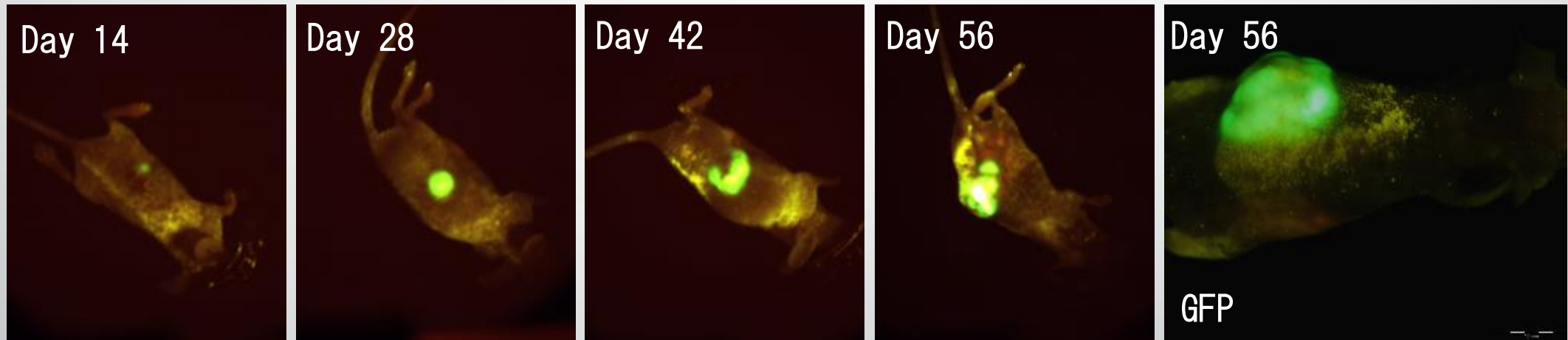
Various SOI models are available.



“Implantation of human tumor tissue into the corresponding organ of mouse”

## SOI model

Ovarian cancer Cell line: SKOV3-GFP

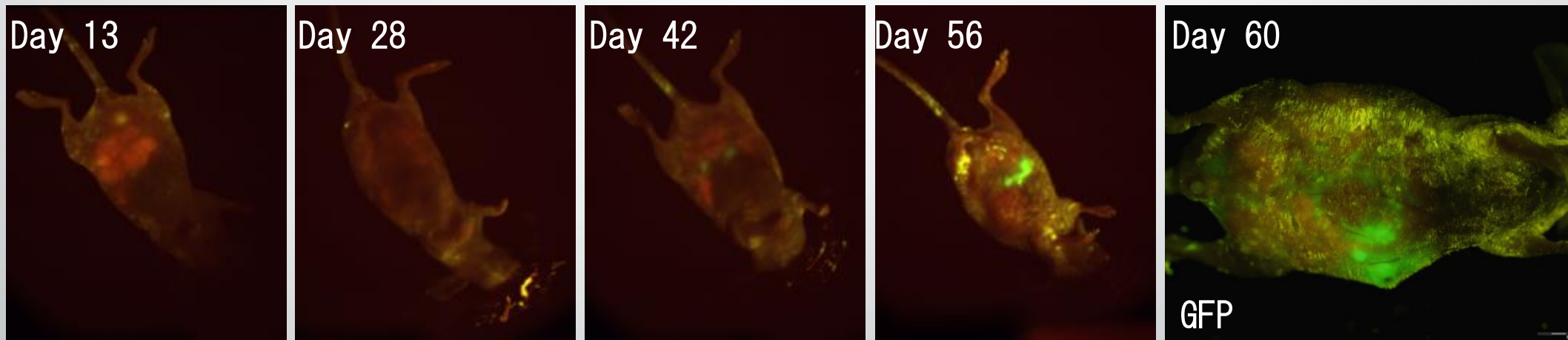


Various SOI models are available.

“Implantation of human tumor tissue into the corresponding organ of mouse”

## SOI model

Stomach cancer Cell line: NUGC4-GFP

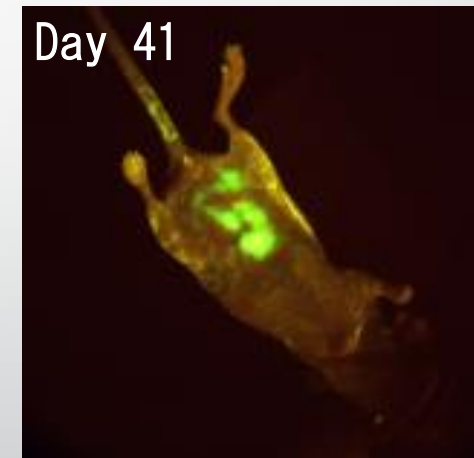
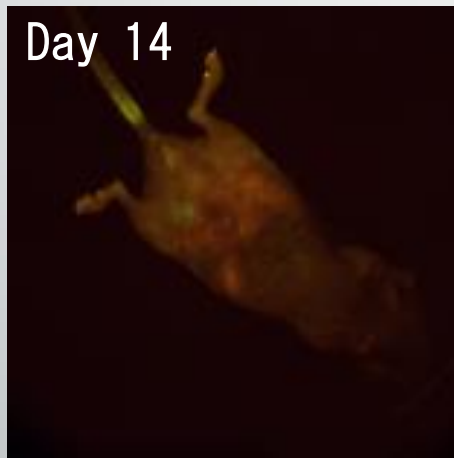


Various SOI models are available.

“Implantation of human tumor tissue into the corresponding organ of mouse”

## SOI model

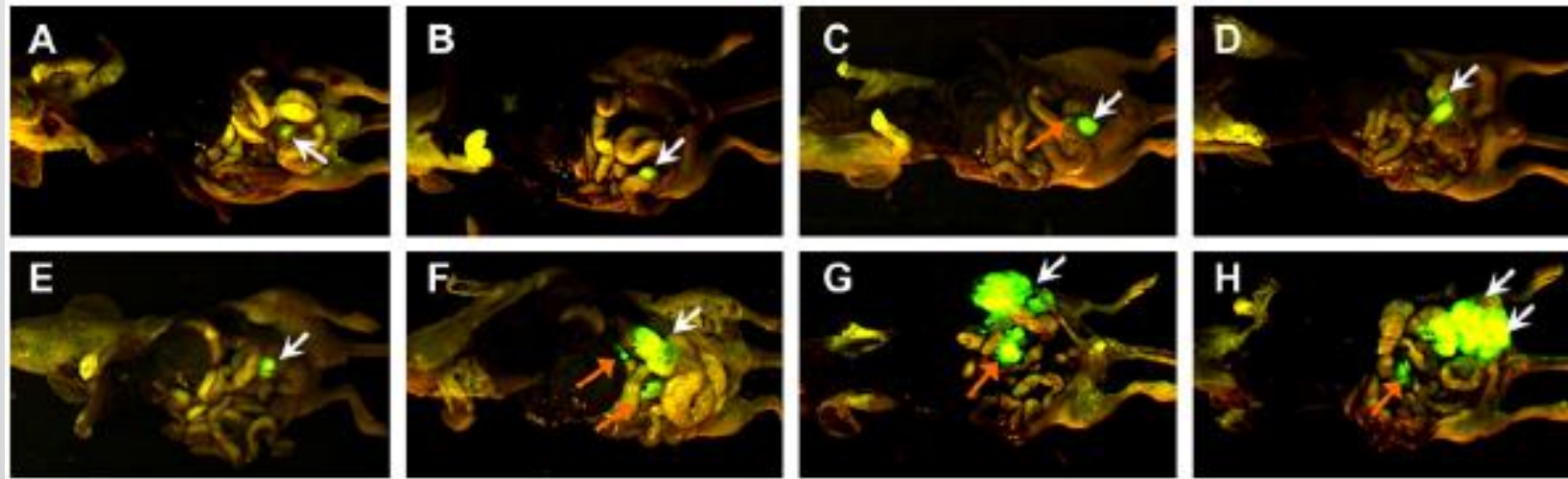
Colon cancer Cell line: HCT-116-GFP



Various SOI models are available.

# Evaluation of anticancer drug efficacy in **SOI** model

Colon cancer Cell line: HT29-GFP

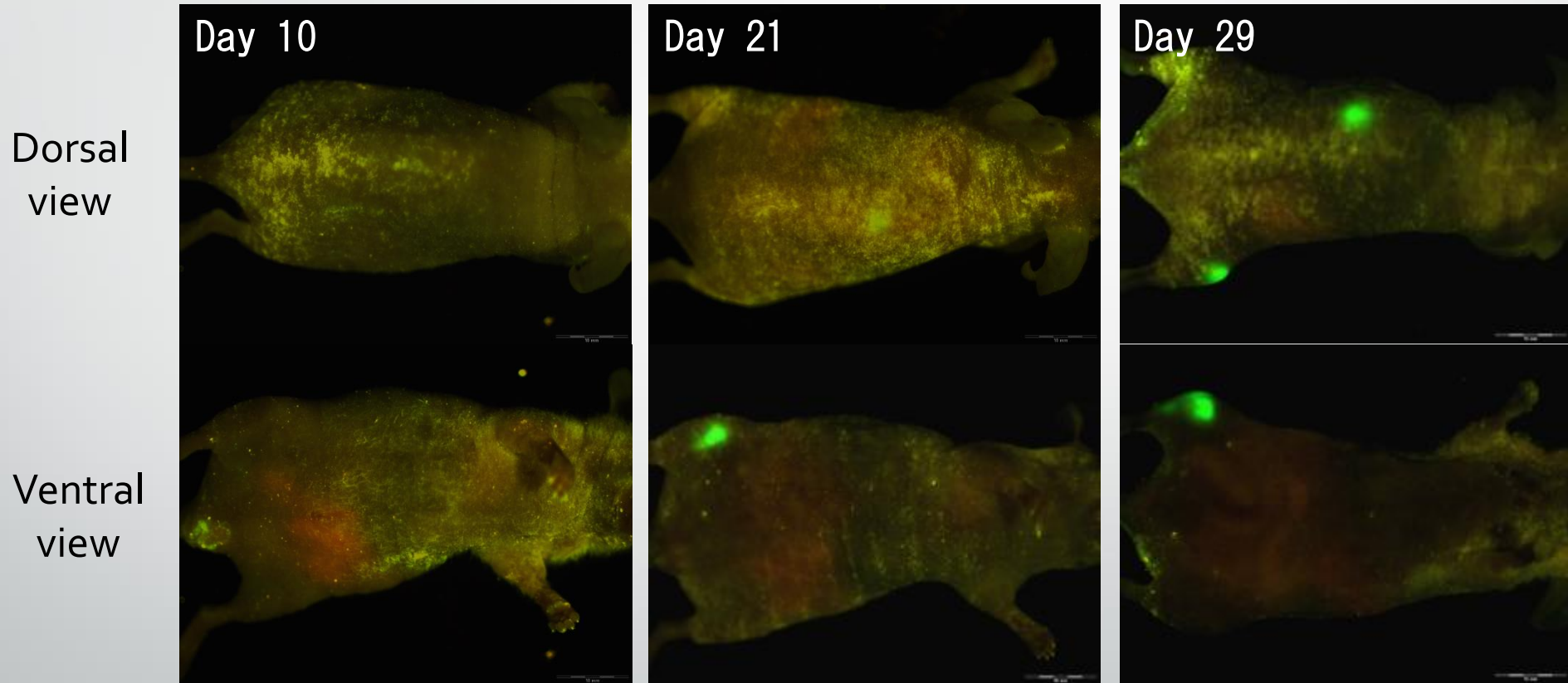


	A	B	C	D	E	F	G	H
Treatment	MEN4901/T-0128					Irinotecan		Untreated
	1760 mg/kg, single	880 mg/kg, q7d x 2	880 mg/kg, single	440 mg/kg, q7d x 2	440 mg/kg, q4d x 4	80 mg/kg, q4d x 4	40 mg/kg, q4d x 4	
Inhibition rate (%)	80.4	81.5	70.7	80.4	84.8	56.5	22.8	–

(Ma *et al*, *J. Surgical Res.*, 2011)

# Leukemia TVI model

Leukemia Cell line: U937-GFP

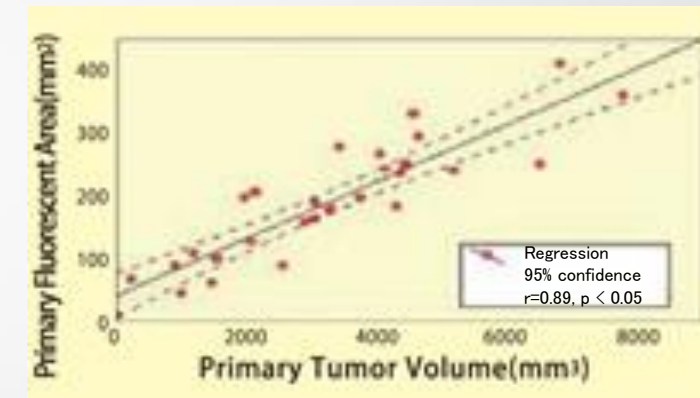
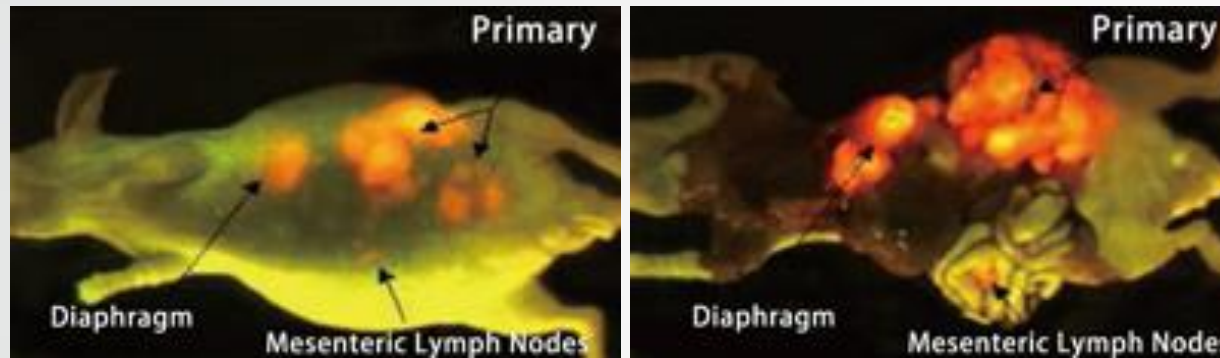


**Bone metastases of leukemia were observed.**



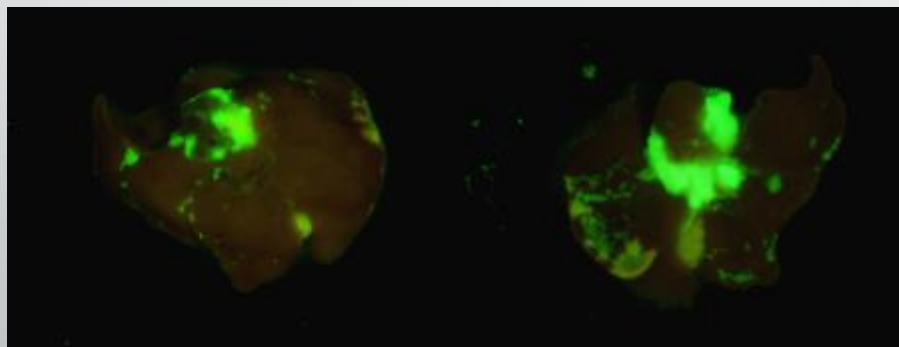
# Cancer studies by fluorescent imaging

- Correlation between fluorescent area and tumor volume

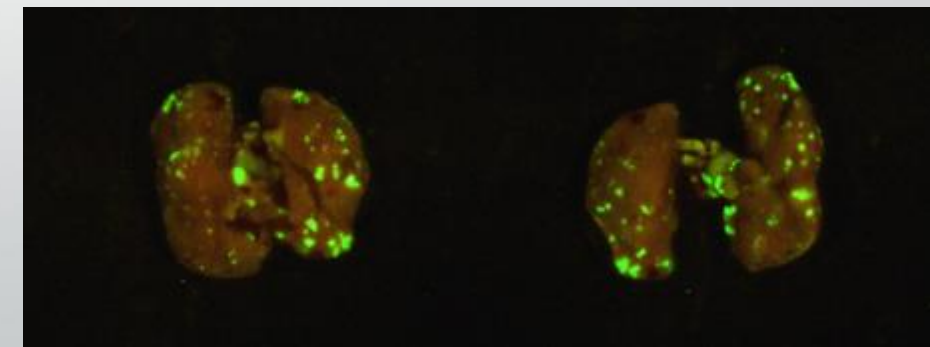


(Katz *et al*, *J. Surgical Res.*, 2003)

- Detection of micro-metastasis



Liver

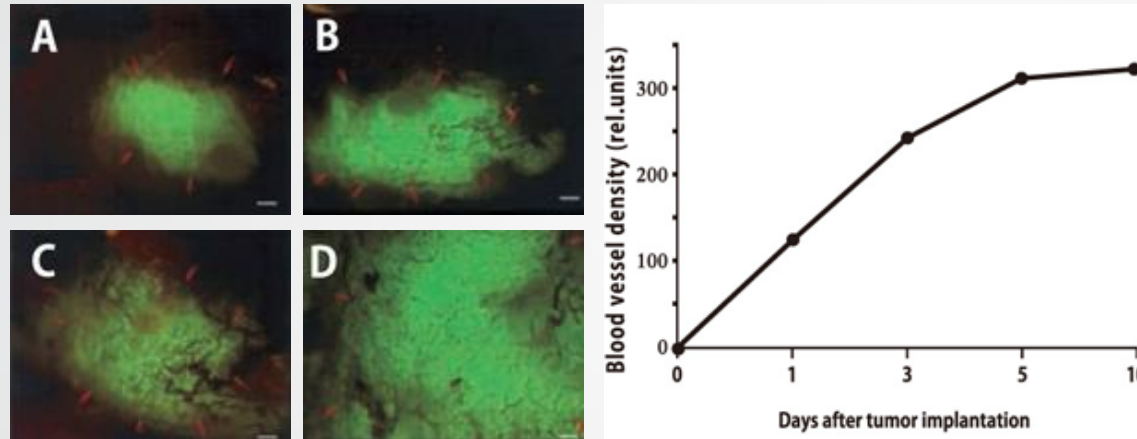


Lung



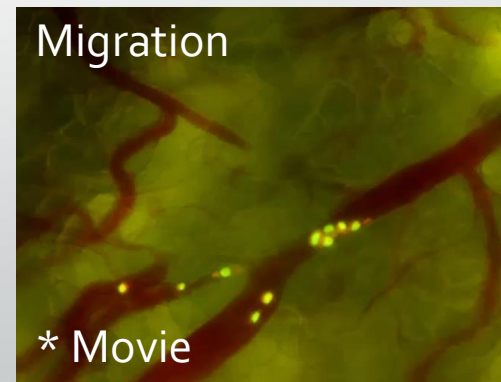
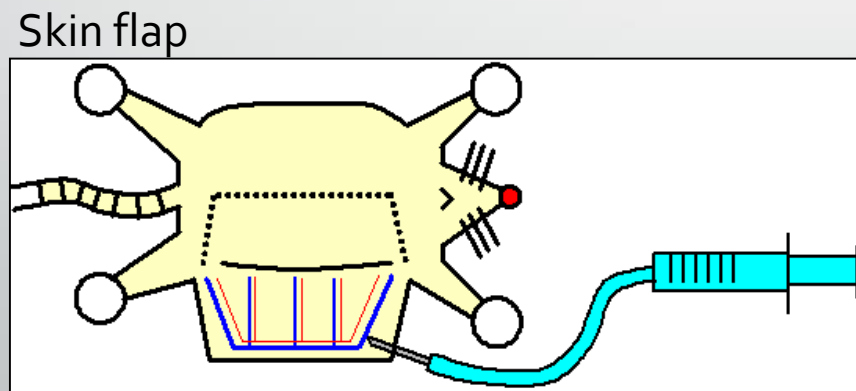
# Cancer studies by fluorescent imaging

- Time course of angiogenesis



(Yang *et al*, *PNAS.*, 2001)

- Vascular migration of cancer cell



AntiCancer's SOI mouse model is....

**Growth and metastasis model of human cancer**

**Available model of various human cancers**

- Colon, Stomach, Pancreas, Breast, Ovary, Bladder, Prostate -  
(TVI model are used in case of Lung cancer, Leukemia, Melanoma )

**Less invasive method**

# Fluorescent imaging systems

17/21



NIPPON ROPER  
Lumazone FL



UVP iBOX



OLYMPUS OV110

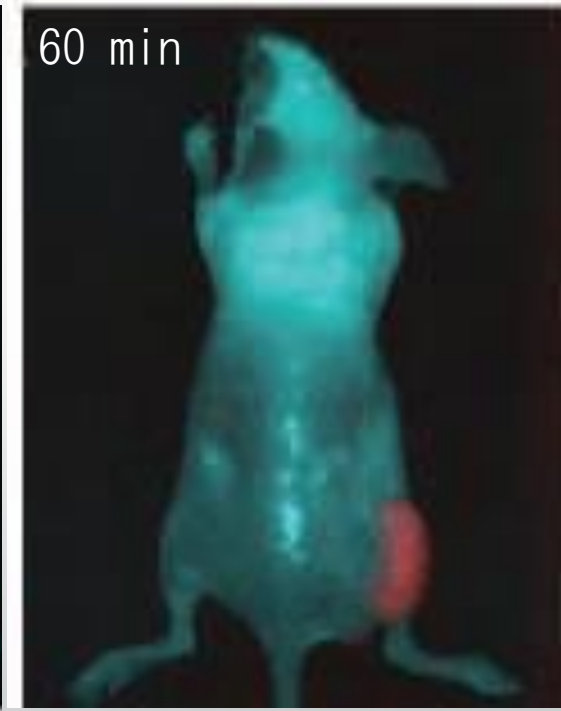
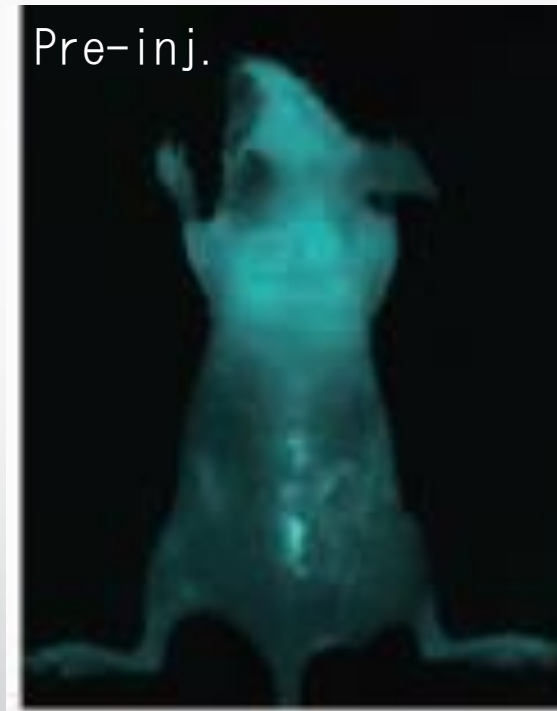
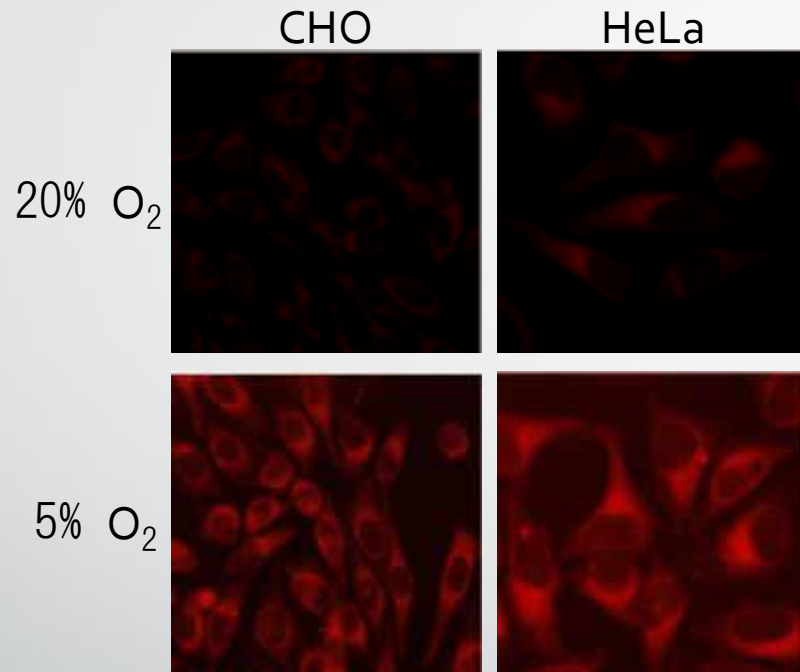


INDEC Biosystems  
FluorVivo100

# Our challenges for advanced imaging research

## 1. Near infrared (NIR) probes for cancer

- BTP derivatives (Zhang *et al*, *Cancer Res.*, 2010)



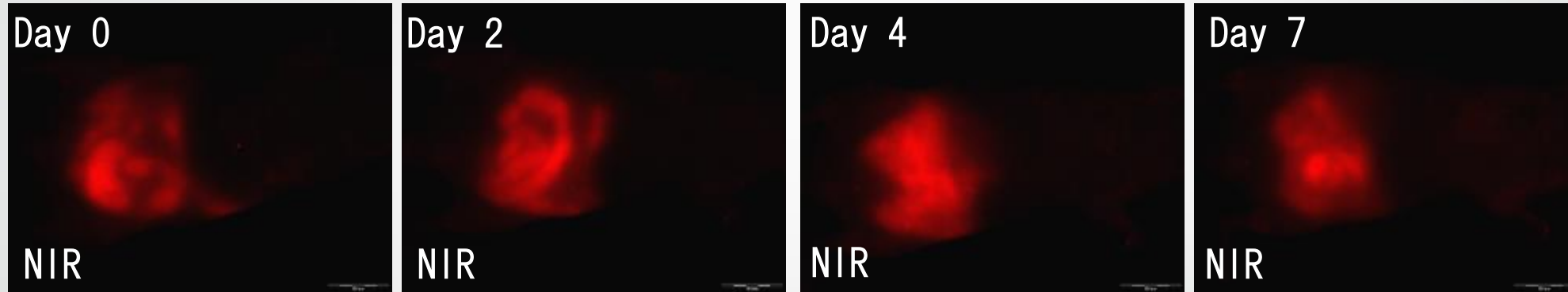
Excitation: 575–675 nm  
Emission : > 645 nm

# Our challenges for advanced imaging research

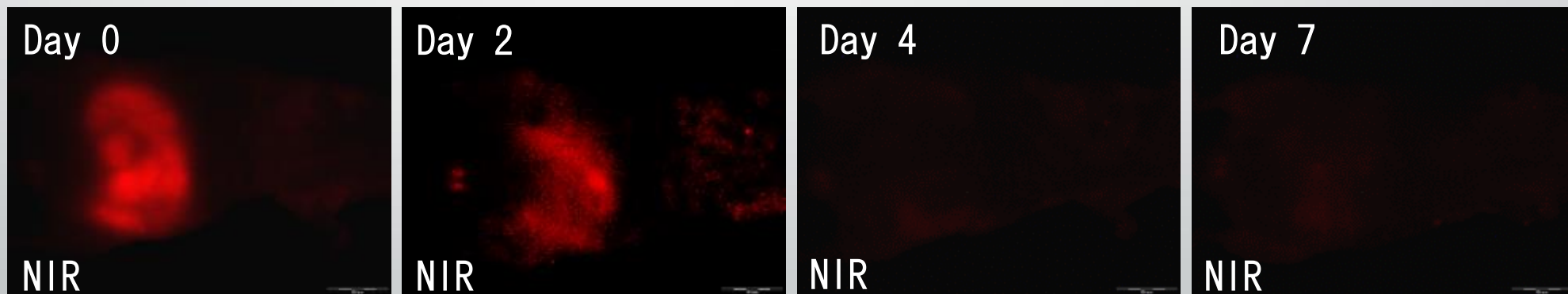
## 2. Sensitivity improvement of fluorescent signal

- Usage of low fluorescent diet

Normal diet

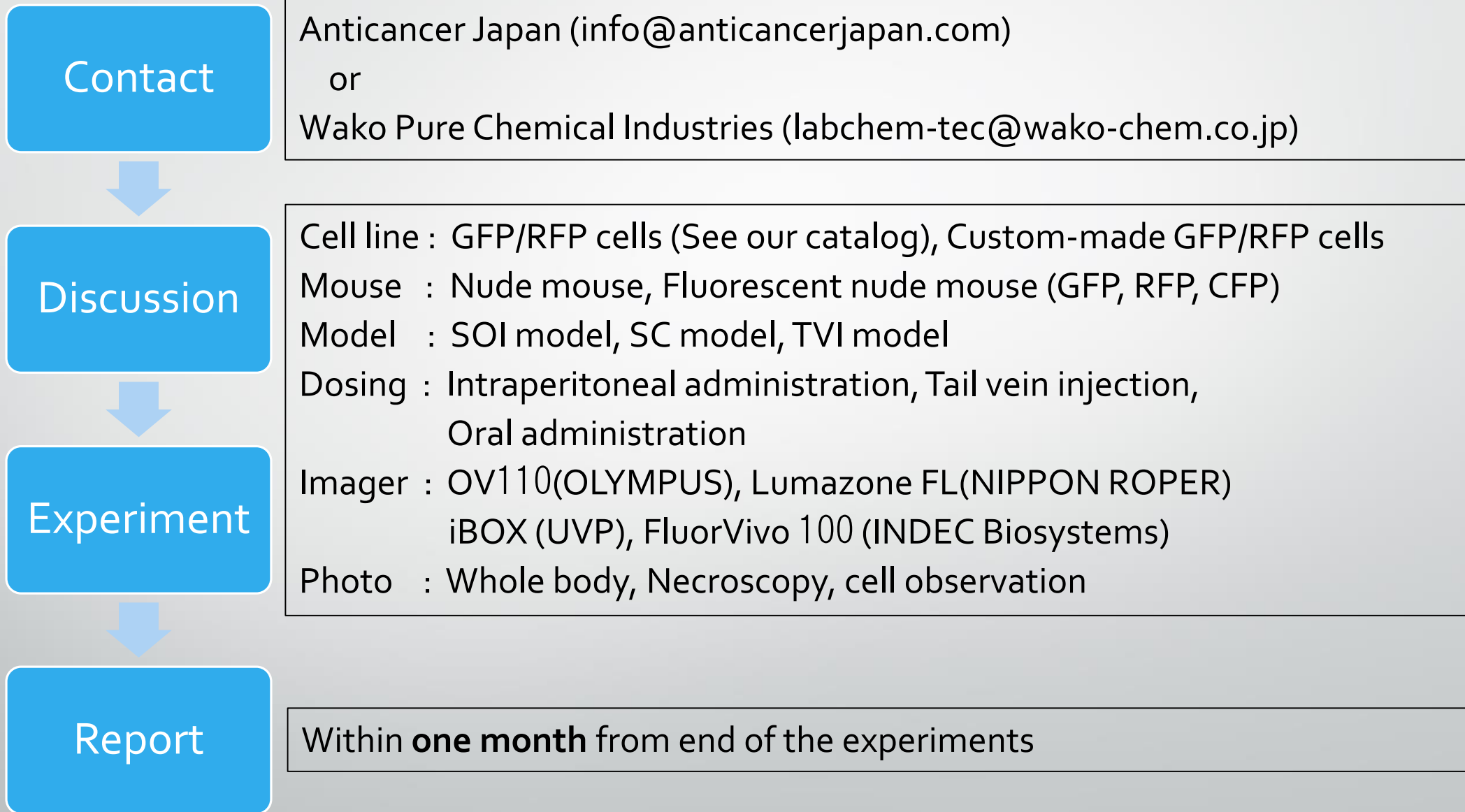


Low-fluorescent diet \* CE-2 (without alfalfa) (CLEA Japan Inc.)



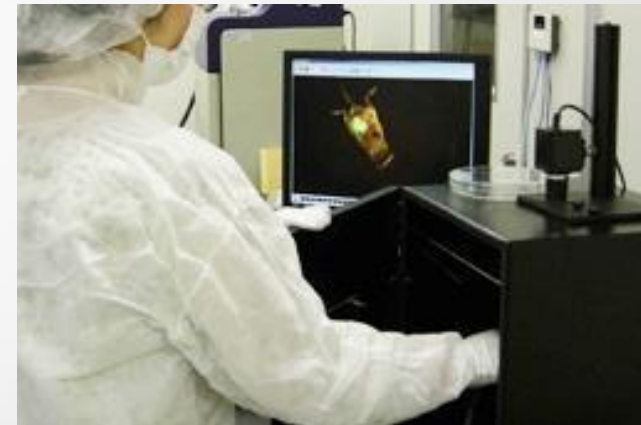
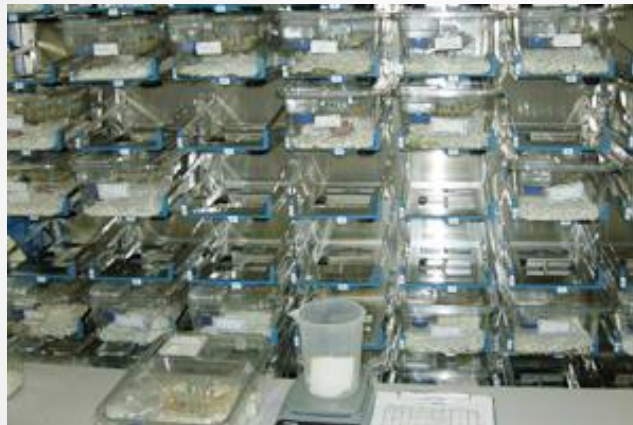
**Intrinsic NIR fluorescence decreased.**

# Flow of contract research





# Please visit to Wako pavilion in BIOtech 2013 and Anticancer Japan's Saito lab.



## Contact to AntiCancer Japan

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