# 東京大学小児外科講座開設25周年記念講演会

（2014年6月8日、東京）

# 変わる技・変わらぬ心

## ―東大小児外科の先生とやってきた研究を通じて―


Eiji Kobayashi, MD, PhD
Department of Organ Fabrication,
Keio University School of Medicine, Japan


1992年　大分別府の温泉旅館にて
92 1 28

# Experimental orthotopic liver transplantation using TOM-2H solution, in which the major anion is gluconate: a preliminary report.

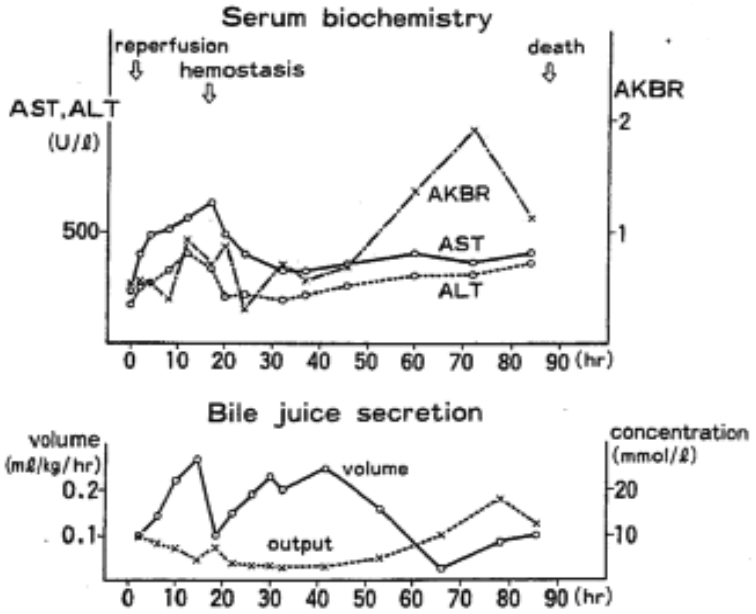
**Iwanaka T**, Kawarasaki H, Hashizume K, Kanamori Y, Tanaka K, Utsuki T, Komuro H, Sugiyama M, Uno T, Tsuchida Y **Kobayashi E** and Hiroki S

Transplant Proc. 1992 Aug;24(4):1602-4.

**Table 1. OLT Using TOM-2H Solution in Japanese Monkeys**

| Case | Preservation Time (Hours : Minutes) | Prognosis | Survival Time (Hours) | Cause of Death |
|---|---|---|---|---|
| 1 | 24 : 28 | Survived | 27 | Accidental splenic rupture |
| 2 | 25 : 31 | Died | — | Surgical error |
| 3 | 25 : 18 | PNF* | 10 | Intraoperative bleeding |
| 4 | 27 : 41 | Died | — | Multiple portal embolism |
| 5 | 25 : 53 | Survived | 87 | Hypovolemic shock |
| 6 | 26 : 42 | PNF* | 12 | Postoperative bleeding |

*Primary nonfunction of graft.



# 1997年　第43回日本移植学会総会（鹿児島）にて


2000年 臓器置換研究部にて


2001年　河原崎教授チームによる
小児生体肝移植プログラム開始

# プロジェクト X

- I 実験マイクロサージャリープロジェクト
- II トランスジェニックラットプロジェクト
- III 再生医学(もの作り)プロジェクト
- IV DNA遺伝子導入プロジェクト
- V 免疫制御プロジェクト
- VI ピッグラボプロジェクト
- VII ピッグラボプロジェクト
- VIII ひとモノ研究プロジェクト
- IX ネコ腎移植プロジェクト
- X トランスジェニックラットプロジェクト

再生医学(もの作り)プロジェクト

ピッグラボプロジェクト

トランスジェニックラットプロジェクト

小林英司:自治医科大学臓器置換研究部(2000－2009年)

# 移植臓器の
# 自助努力の方向性

2006年　厚生労働省　班長
2007年　TTSかじ取り委員

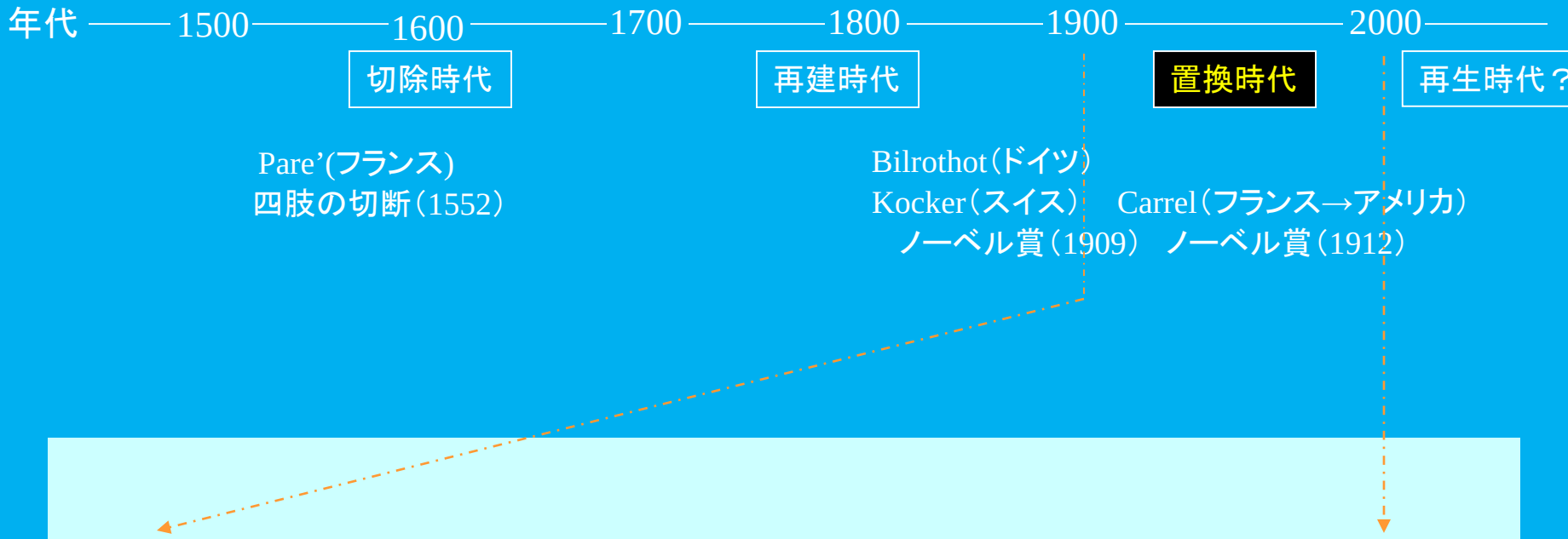

参議院会議
（2009年7月6日）


（Lancet 2008）

2008年　イスタンブール宣言
2009年　移植法案改正

# ‘移植可能な臓器を作る’計画

# 変わりゆく外科技術




1900 — 2000

（1902）
**Carrel**
臓器移植の実験

（1952）
**Elion**
アザチオプリン発現

（1956）
**Medawer**
のマウス皮膚移植実験

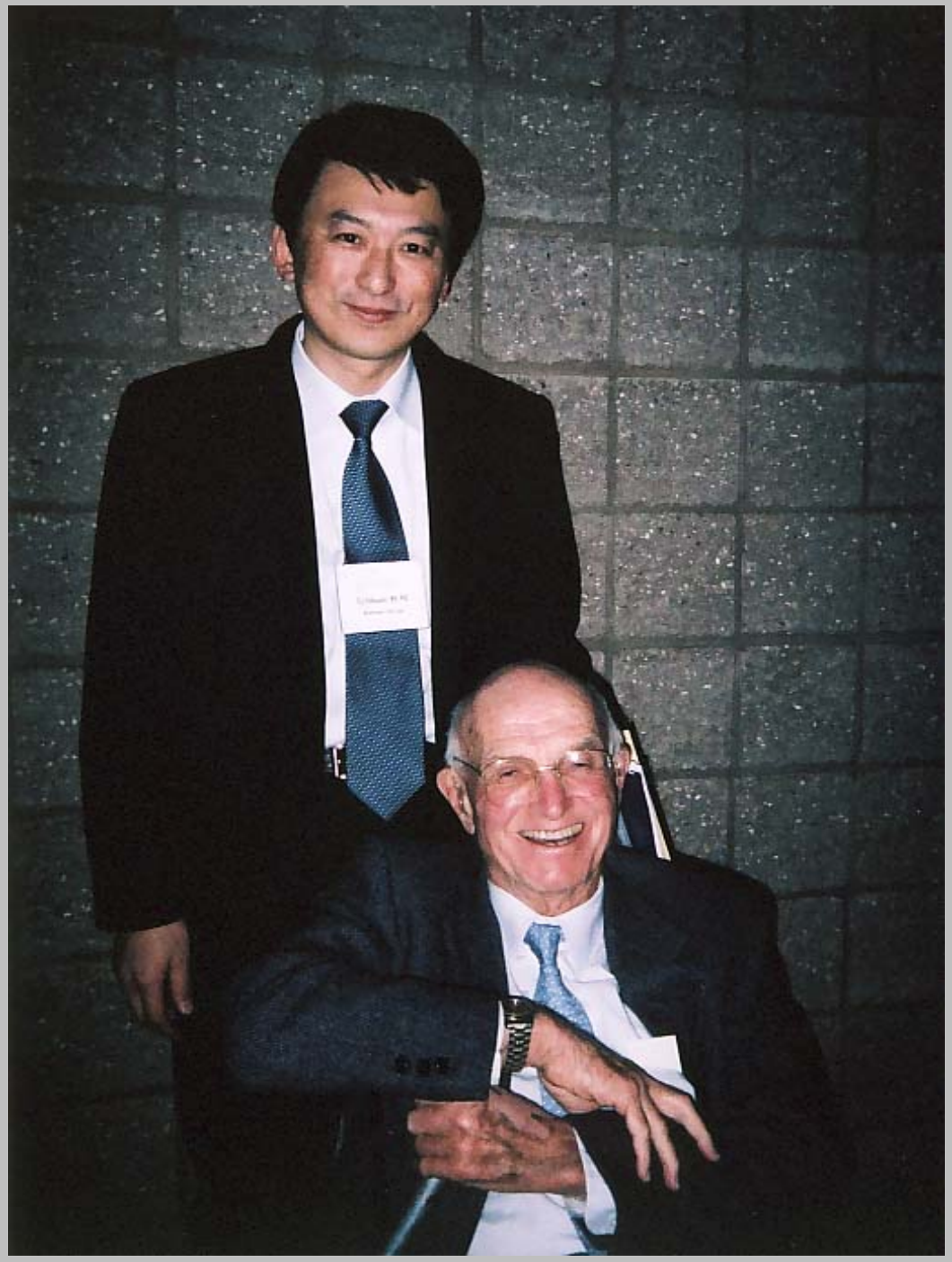
（1960）
**Murry**
臨床腎移植

（1970）
Borel
シクロスポリン発見

（1978）
**Calne**
シクロスポリン使用
腎移植

（1989）
Kino
タクロリムス発見

（1990）
**Starzl**
タクロリムス使用
移植



# 自治医科大学生体肝移植チームの変遷

2001年　自治医科大学外科学講座　小児外科・移植外科新設
河原崎秀雄教授・水田助手 就任
第1例目生体肝移植（5月22日）


2007年　第100例目生体肝移植

2008年　国内最年少新生児肝移植成功
（日齢17日、体重2.6kg）

2009年　河原崎秀雄教授　退職、
小林英司教授　転出
水田移植外科准教授昇進

2010年　腹腔鏡補助下ドナー肝切除　導入
脳死肝移植認定施設（18歳未満限定、全国22施設）

2011年　第200例目生体肝移植（小児施設では本邦初）
脳死小腸移植認定施設（全国13施設）

（水田先生より）

Mizuta K, Jichiでヒット

Pretransplant Levels of Endotoxin Can Predict the Risk of Bacterial Infections and Graft Liver Function after Liver Transplantation.
Sanada Y, Urahashi T, Ihara Y, Okada N, Yamada N, Hirata Y, **Mizuta K**.
Eur J Pediatr Surg. 2014

Maternal grafts protect daughter recipients from acute cellular rejection after pediatric living donor liver transplantation for biliary atresia.
Sanada Y, Kawano Y, Miki A, Aida J, Nakamura K, Shimomura N, Ishikawa N, Arai T, Hirata Y, Yamada N, Okada N, Wakiya T, Ihara Y, Urahashi T, Yasuda Y, Takubo K, **Mizuta K**.
Transpl Int. 2014

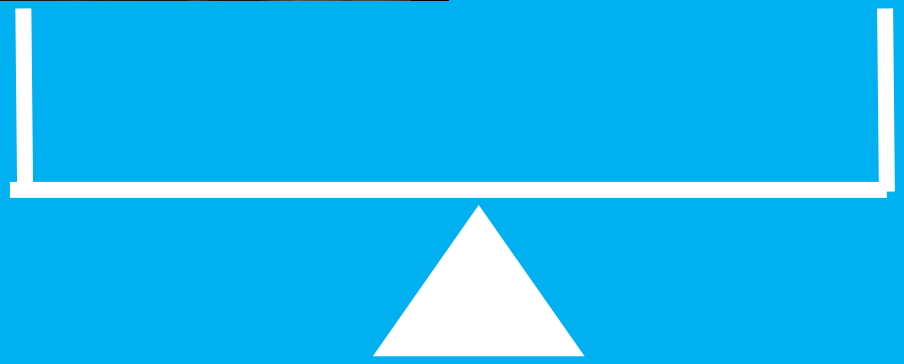
Decreased portal vein flow during Kawasaki disease in a liver transplant patient.
Wakiya T, Urahashi T, Ihara Y, Sanada Y, Yamada N, Okada N, Hakamada K, **Mizuta K**.
Pediatr Int. 2013

Effect of repeat Kasai hepatic portoenterostomy on pediatric live-donor liver graft for biliary atresia.
Urahashi T, Ihara Y, Sanada Y, Wakiya T, Yamada N, Okada N, **Mizuta K**.
Exp Clin Transplant. 2013

# 低侵襲外科への流れ

内視鏡外科手術

開腹外科手術




1999年　臨床薬理学教室にて
BJCP
BJCP
内科学
FILE

**Uchida H, Saitamaでヒット**

Laparoscopic excision of urachal remnants is a safe and effective alternative to open surgery in children.
Masuko T, **Uchida H**, Kawashima H, Tanaka Y, Deie K, Iwanaka T.
J Laparoendosc Adv Surg Tech A. 2013

External stabilization for severe tracheobronchomalacia using separated ring-reinforced ePTFE grafts is effective and safe on a long-term basis.
Takazawa S, **Uchida H**, Kawashima H, Tanaka Y, Masuko T, Deie K, Nagase Y, Iwanaka T.
Pediatr Surg Int. 2013

Single-incision laparoscopic-assisted appendectomy in children: exteriorization of the appendix is a key component of a simple and cost-effective surgical technique.
Deie K, **Uchida H**, Kawashima H, Tanaka Y, Masuko T, Takazawa S.
Pediatr Surg Int. 2013

Complete thoracoscopic versus video-assisted thoracoscopic resection of congenital lung lesions.
Tanaka Y, **Uchida H**, Kawashima H, Sato K, Takazawa S, Masuko T, Deie K, Iwanaka T.
J Laparoendosc Adv Surg Tech A. 2013

「セカンド・オーサー
では教授になれない？」

# CHANGES IN IMMUNE-ENDOCRINE RESPONSE AFTER SURGERY

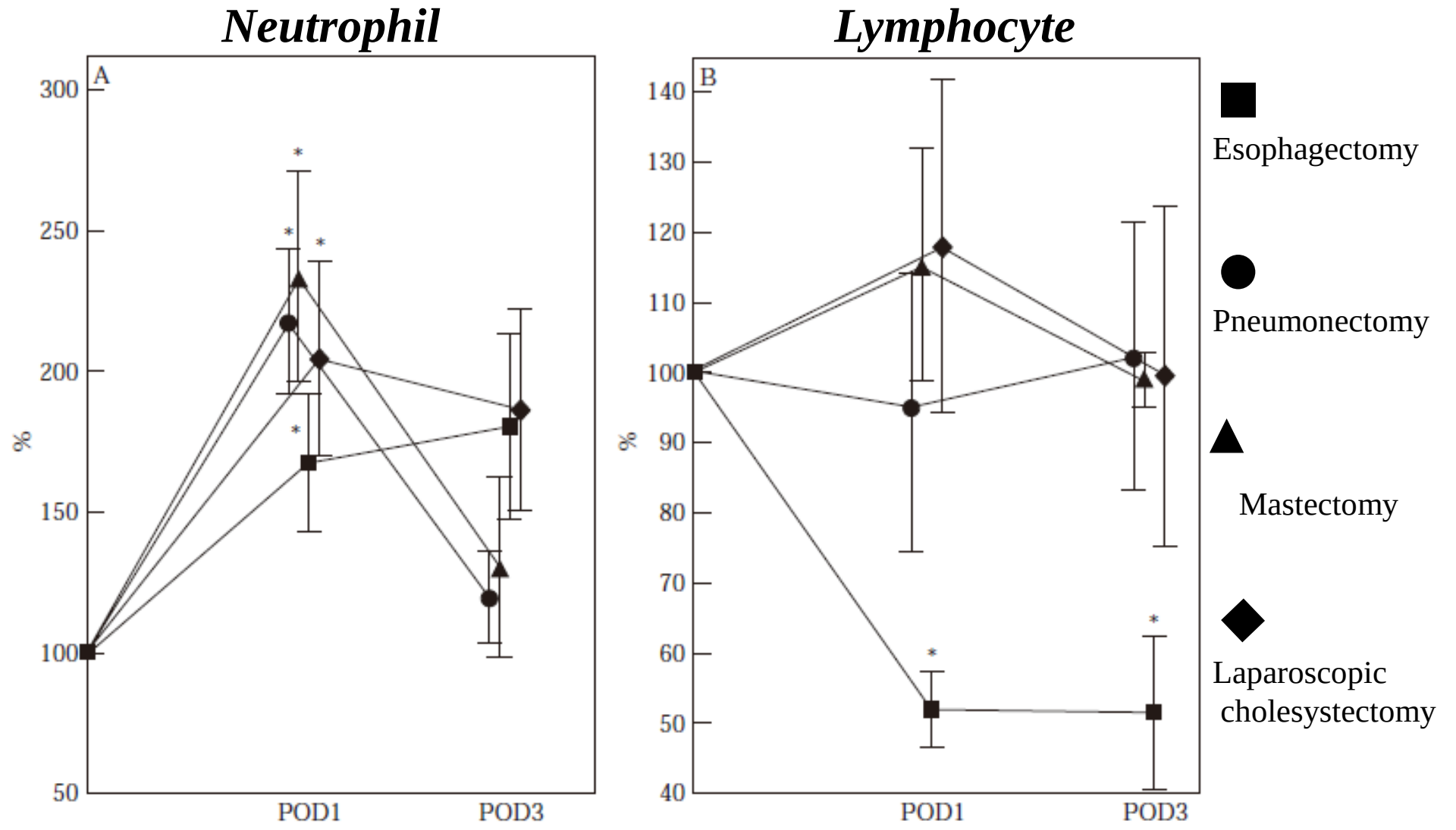
**TABLE 1. Patient's characteristics and surgical procedure**

| Operation (group) | *n* | Age (year) | Operating time (min) | Loss of blood (cc) |
|---|---|---|---|---|
| Thoracic oesophagectomy (O group) | 7 | 61.4 ± 2.4 | 495.0 ± 24.9 | 1295.7 ± 446.6 |
| Plumomary lobectomy (P group) | 5 | 70.0 ± 5.2 | 306.0 ± 26.2 | 368.0 ± 50.1 |
| Modified mastectomy (M group) | 7 | 50.6 ± 5.1 | 175.0 ± 22.4 | 172.5 ± 22.2 |
| Laparoscopic cholecystectomy (LC group) | 5 | 45.7 ± 4.5 | 107.0 ± 8.5 | uncountable |

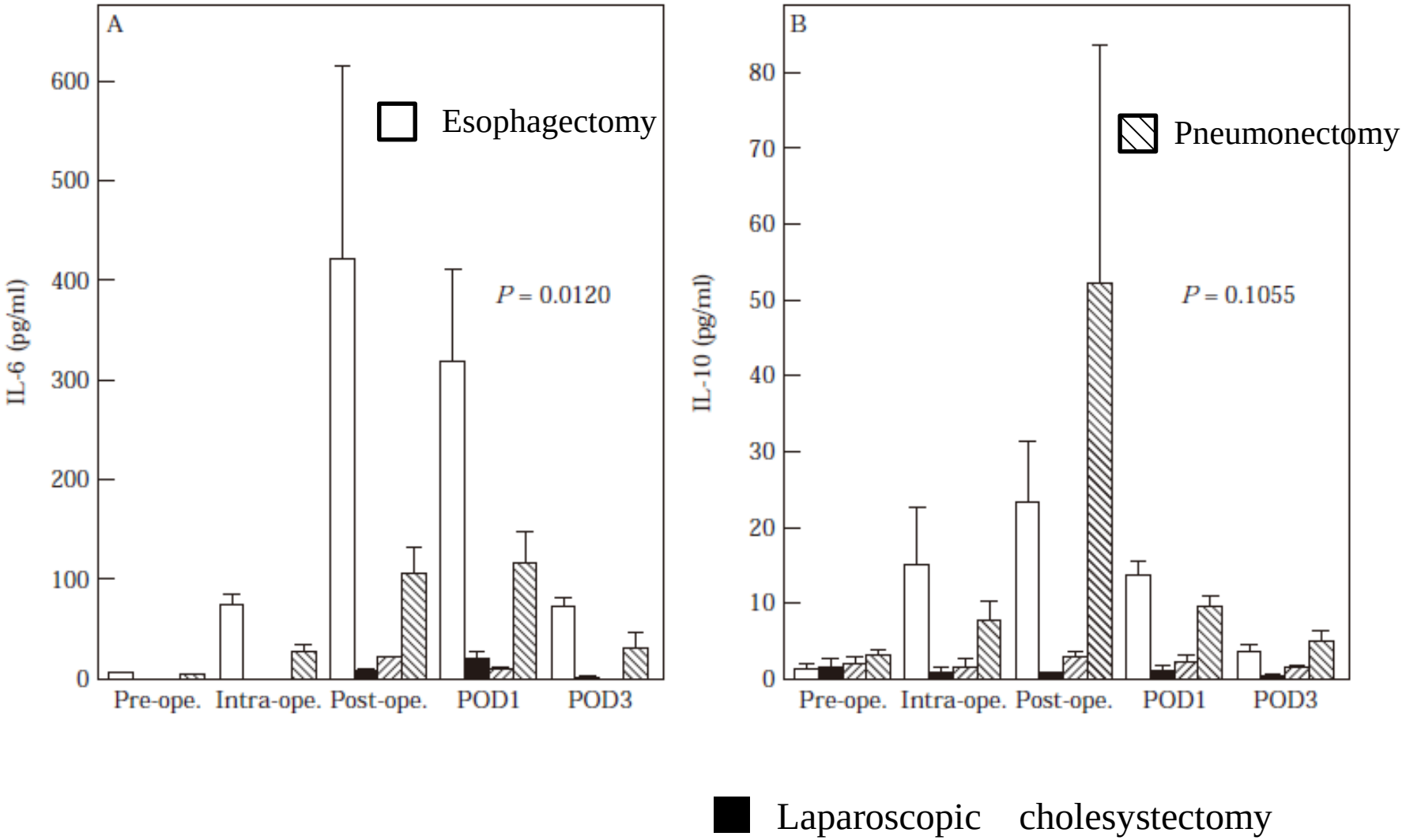
Data are expressed as mean ± SEM.

*(Yamauchi H, **Kobayashi E**, et al. Cytokine 1998)*

# Change of neutrophil and lymphocyte numbers after operation



# The changes of serum cytokine (IL-6 and IL-10) levels after surgery



# Hormone-cytokine response

## Pneumoperitoneum vs abdominal wall-lifting in laparoscopic cholecystectomy

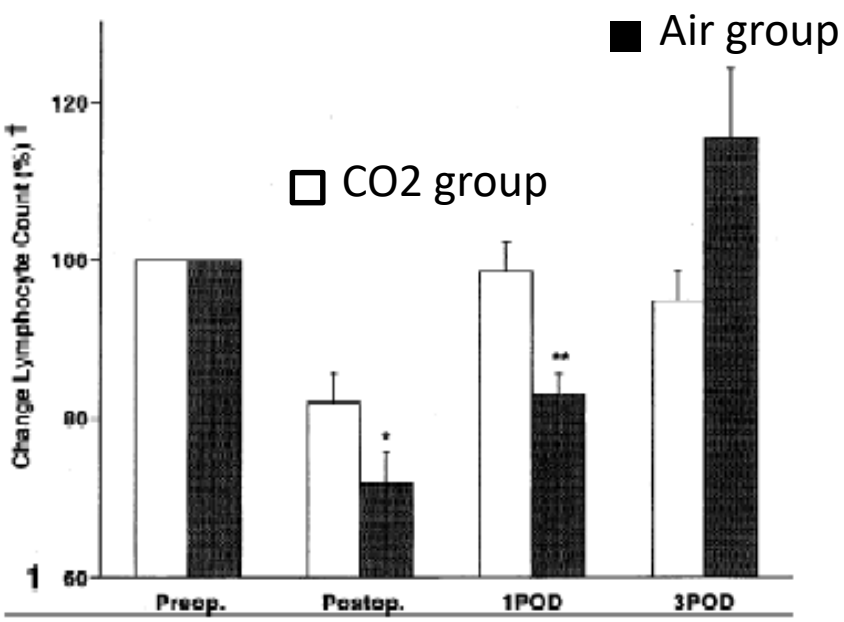
**Table 1.** Patient characteristics and clinical parameters[a]

| | Mean [SEM] | | |
|---|---|---|---|
| | $CO_2$ group ($n = 9$) | Air group ($n = 8$) | $p =$ [b] |
| Age (years) | 47.7 [3.7] | 50.5 [2.7] | 0.700 |
| Height (cm) | 158.0 [1.0] | 155.3 [1.6] | 0.498 |
| Weight (kg) | 54.7 [2.6] | 61.6 [3.4] | 0.149 |
| Operation time (min) | 114.4 [9.3] | 121.3 [8.8] | 0.562 |
| Anesthesia time (min) | 198.9 [10.7] | 202.5 [5.3] | 0.923 |
| Pentazocine request (times) | 1.1 [0.4] | 1.4 [0.5] | 0.689 |
| Time to full diet (days) | 1.7 [0.1] | 1.8 [0.2] | 0.804 |
| Hospital stay (days) | 6.0 [0.4] | 6.0 [0.1] | 0.920 |

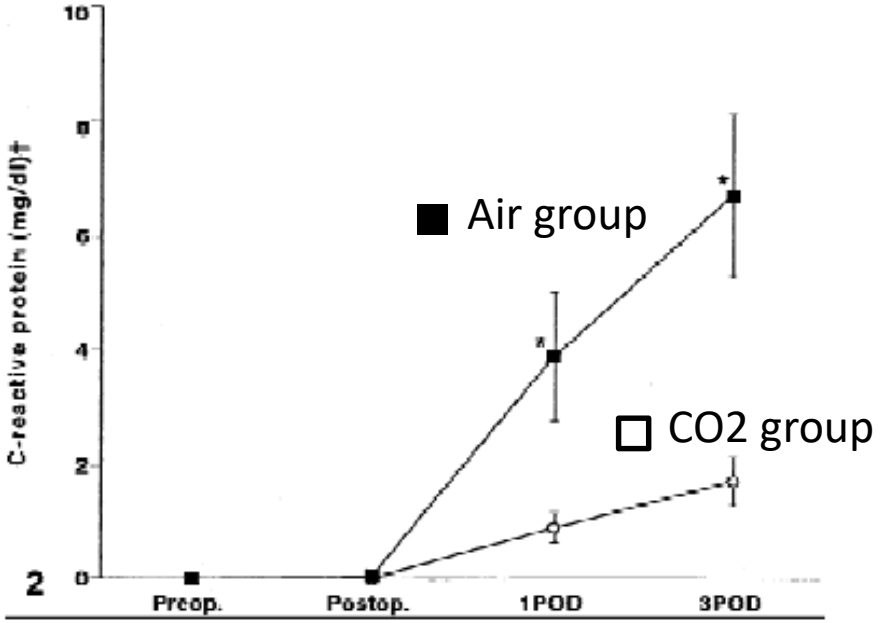
[a] There was no significant difference in all characters and parameters
[b] Mann-Whitney U test

*(Yoshida T, **Kobayashi E**, et al. Surg Endosc 1997)*

# Change of peripheral lymphocyte number and serum C-reactive protein in CO2 vs Air groups over time.

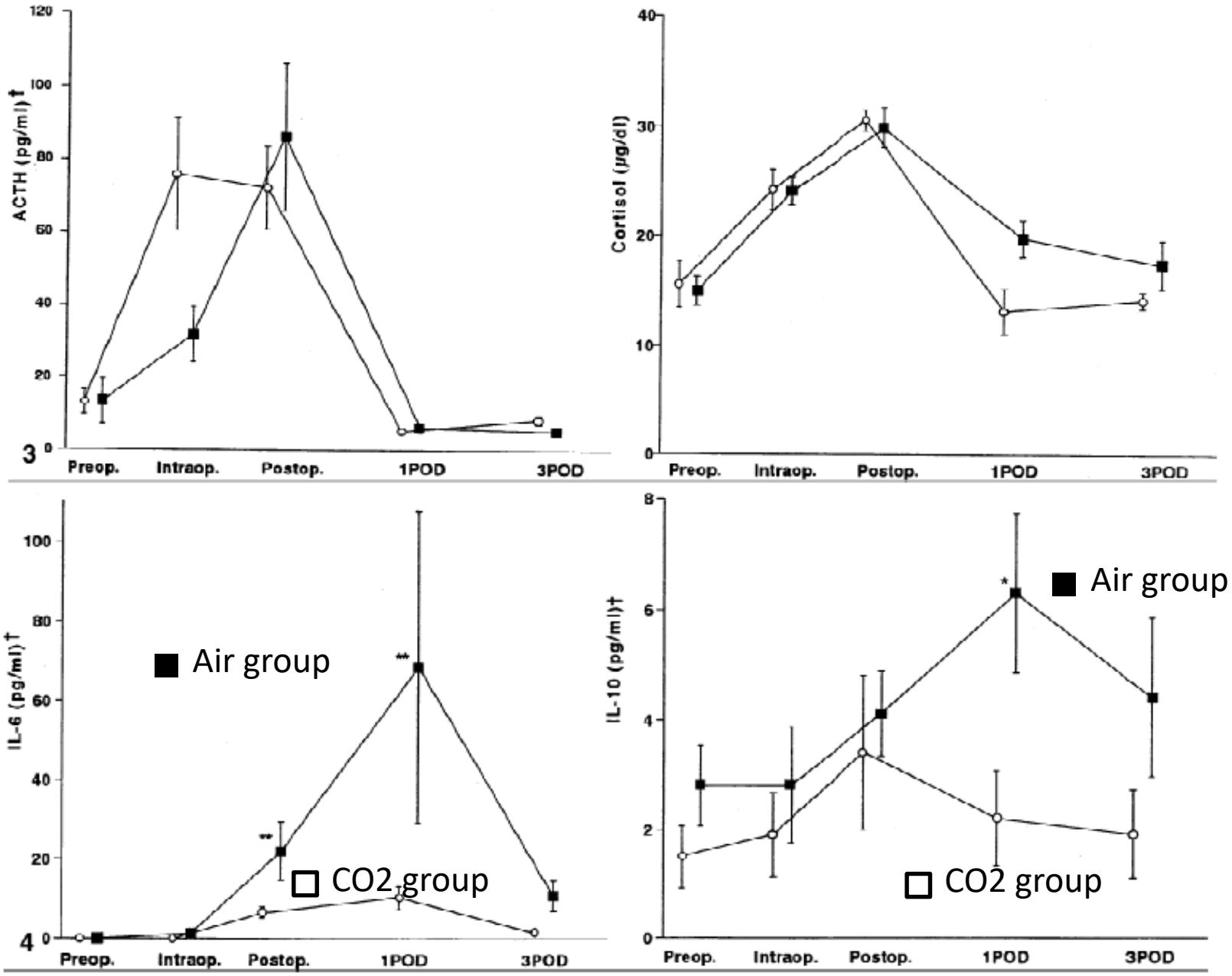



The decrease of lymphocyte number in the Air group was significantly larger than in the CO2 group.




The serum CRP level in the air group was significantly higher than those in the CO2 group.

# The changes of serum hormone and cytokine levels after laparoscopic cholecystectomy



# 実験医学：変わらぬ心

*(**Claude Bernard**; 1813-1878)*

1998年　動物実験室にて

水田・小林　18ヒット

Dose-dependent reduction of bile secretion in cyclosporine-treated rats.
**Mizuta K**, **Kobayashi E**, Uchida H, Fujimura A, Kawarasaki H, Hashizume K.
Transplantation. 1998 Mar 15;65(5):758-9. No abstract available

Influence of tacrolimus on bile acid and lipid composition in continuously drained bile using a rat model. Comparative study with cyclosporine.
**Mizuta K**, **Kobayashi E**, Uchida H, Fujimura A, Kawarasaki H, Hashizume K.
Transpl Int. 1999;12(5):316-22

Cyclosporine inhibits transport of bile acid in rats: comparison of bile acid composition between liver and bile.
**Mizuta K**, **Kobayashi E**, Uchida H, Ogino Y, Fujimura A, Kawarasaki H, Hashizume K.
Transplant Proc. 1999 Nov;31(7):2755-6. No abstract available

Survival of rats undergoing continuous bile drainage depends on maintenance of circadian rhythm of bile secretion.
**Mizuta K**, Hishikawa S, Yoshida T, **Kobayashi E**, Uchida H, Fujimura A, Kawarasaki H, Hashizume K.
Chronobiol Int. 1999 Nov;16(6):759-65

Effect of pretreatment with FTY720 and cyclosporin on ischaemia-reperfusion injury of the liver in rats.
**Mizuta K**, Ohmori M, Miyashita F, Kitoh Y, Fujimura A, Mori M, Kanno T, Hashizume K, **Kobayashi E**.　J Pharm Pharmacol. 1999 Dec;51(12):1423-8

Fluoroquinolone concentrations in plasma, urine, and bile after oral administration in rats with renal failure: useful technique for long-term bile collection.
**Mizuta K**, Hishikawa S, Hirota M, Miyamoto G, Fujimura A, Hakamata Y, **Kobayashi E**.
J Med. 2001;32(5-6):311-20

Increase of bile acid production by tacrolimus in the rat liver.
**Mizuta K**, **Kobayashi E**, Uchida H, Hishikawa S, Kawarasaki H.
Transplant Proc. 2003 Feb;35(1):437-8. No abstract available.

# 新生児小腸が血管吻合がなくても発育する

内田・小林　29ヒット

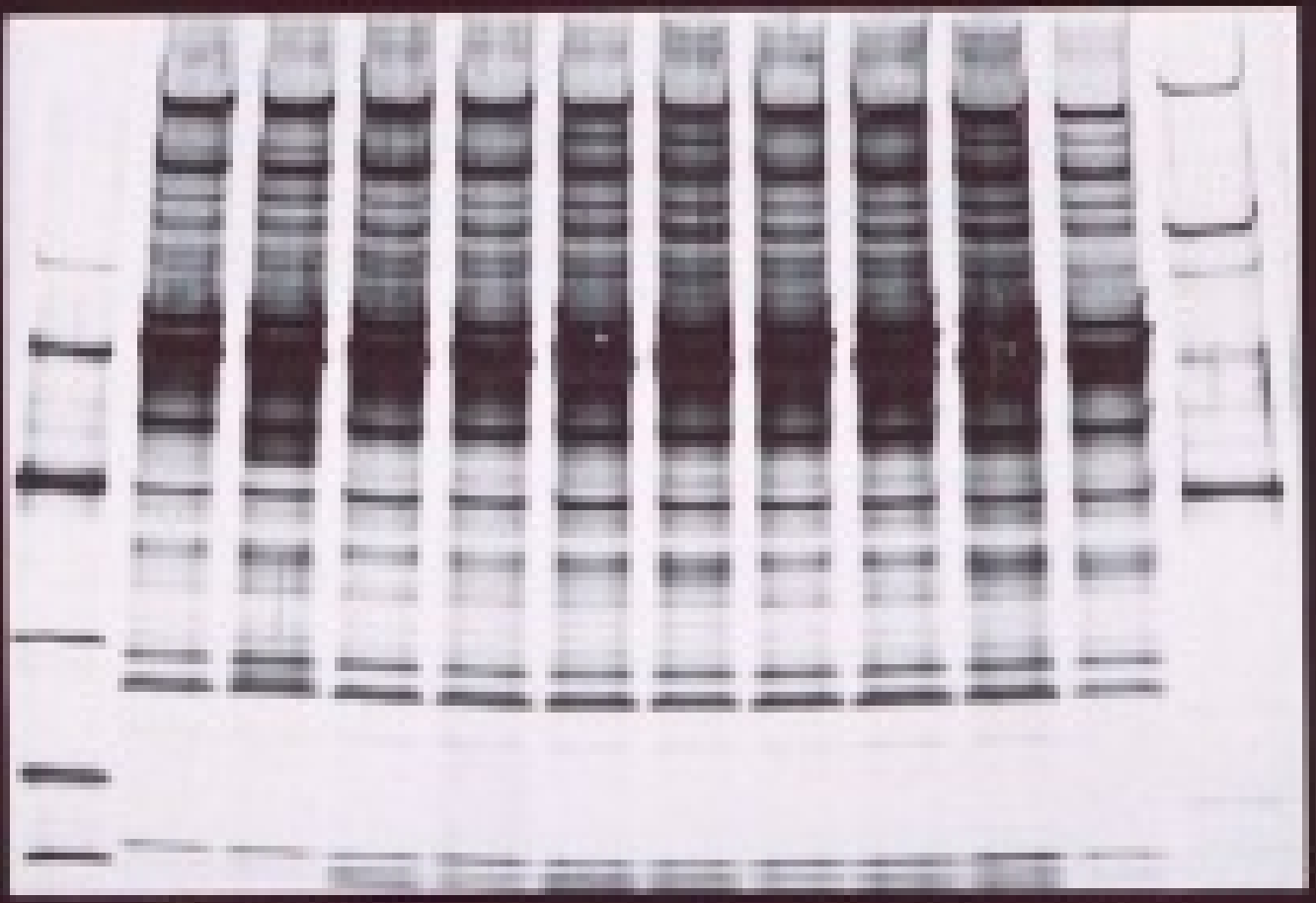
**Experimental Small Bowel Transplantation Using Newborn Intestine in Rats**:
I. Lipid Absorption Restored After Transplantation of Nonvascularized Graft
成長したグラフトで同所置換　(*Uchida H, et al.  J Pedia Surg 1999*)

II. Revascularization of Newborn Intestine Is Independent of Vascular Endothelial Growth Factor92　75　42　25　0 %
脾臓＞小腸＞腎＞心臓＞肝（膵）　*Uchida H, et al.  J Pedia Surg 1999*)

III. Long-Term Cryopreservation of Rat Newborn Intestine
凍 結保存効果（抗原性の失活はない）　(*Tahara K, et al.  J Pedia Surg 2001*)

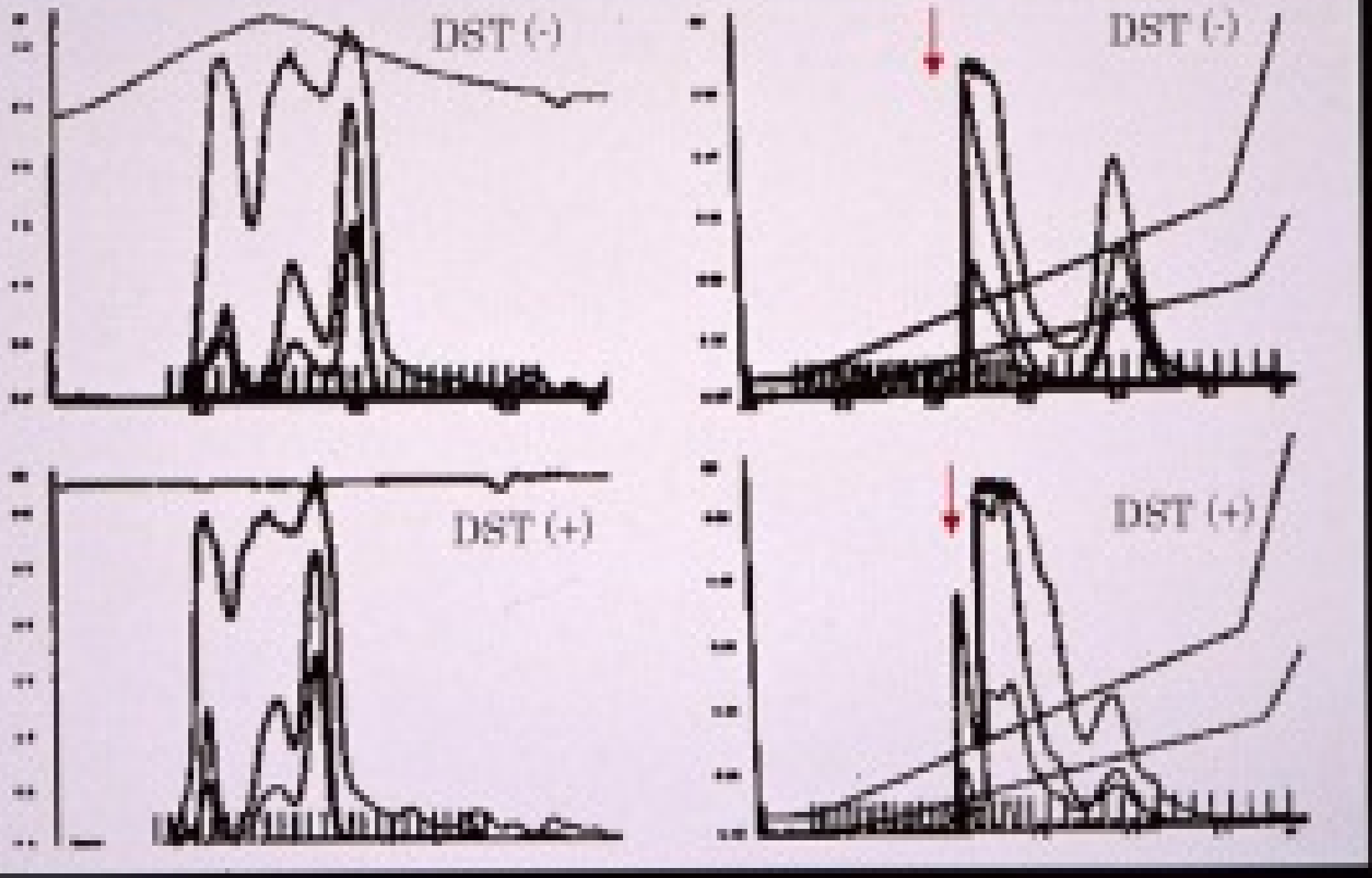
IV. Effect of Cold Preservation on Graft Neovascularization
UW, m-TOM, リンゲル液で保存効果に差なし(*Uchida H, et al.  J Pedia Surg 2001*)

# *Protein finger printings of DST sera by SDS-PAGE*



Gel filtration

Anion exchange



## N-Terminal Sequence of MAY-I

MAY-I:

Rat Inter α Inhibitory H4P Heavy chain:

.....GPPGHPHPASSIDYGRQPSLGR**********GTTP...

## Molecular Size of Purified MAY-I From Sera

MAY-I: 26086.9 Dalton

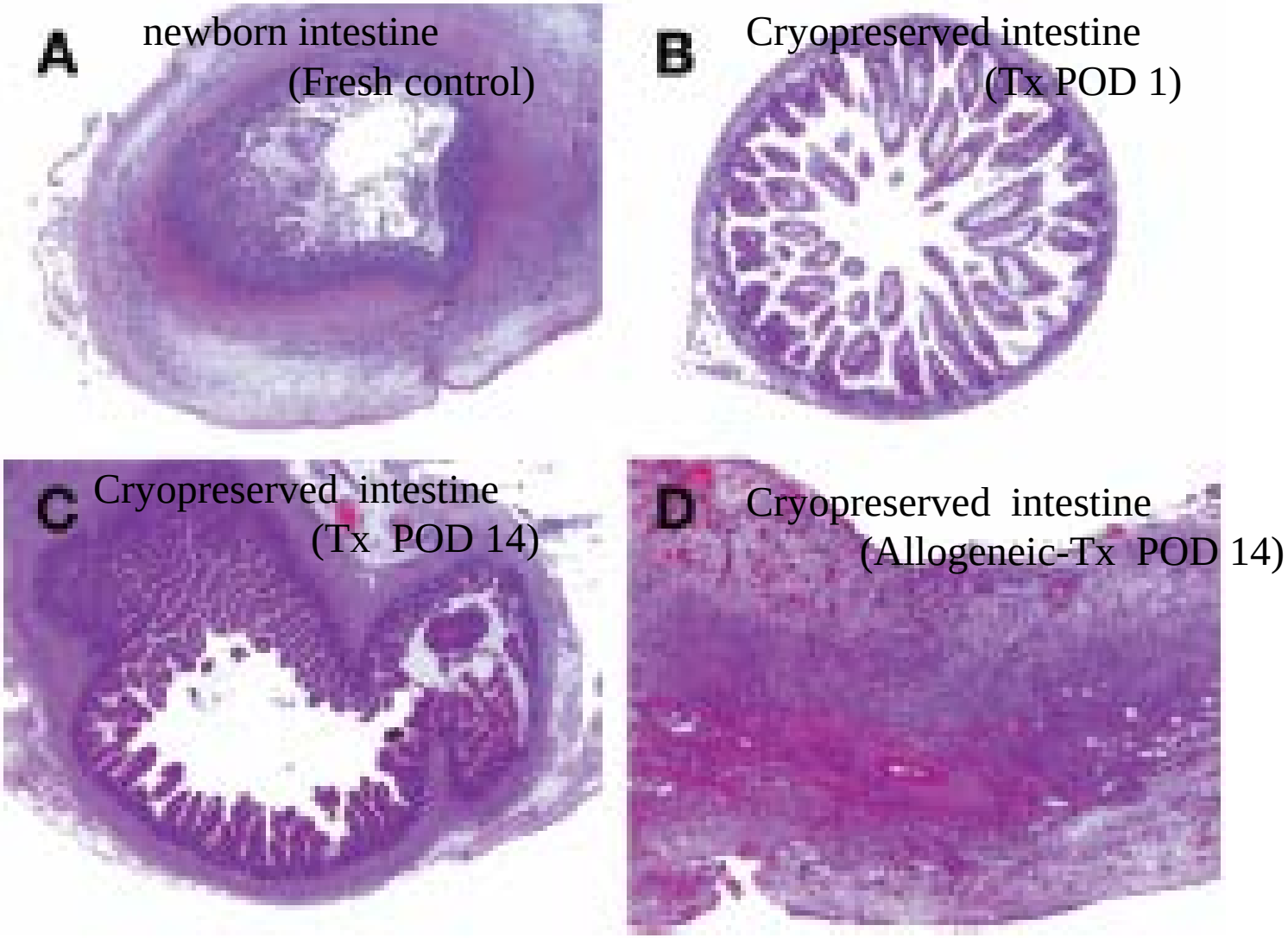
Rat Inter α Inhibitory H4P Heavy chain (234 Amino Acids From C-Terminal): 26080.07 Dalton


***A New Immunosuppressive Factor (MAY-I) Purified from Sera Received Allogeneic Blood Transfusion***

「臨床に通用するマイクロ
サージャリーを教えてください！」

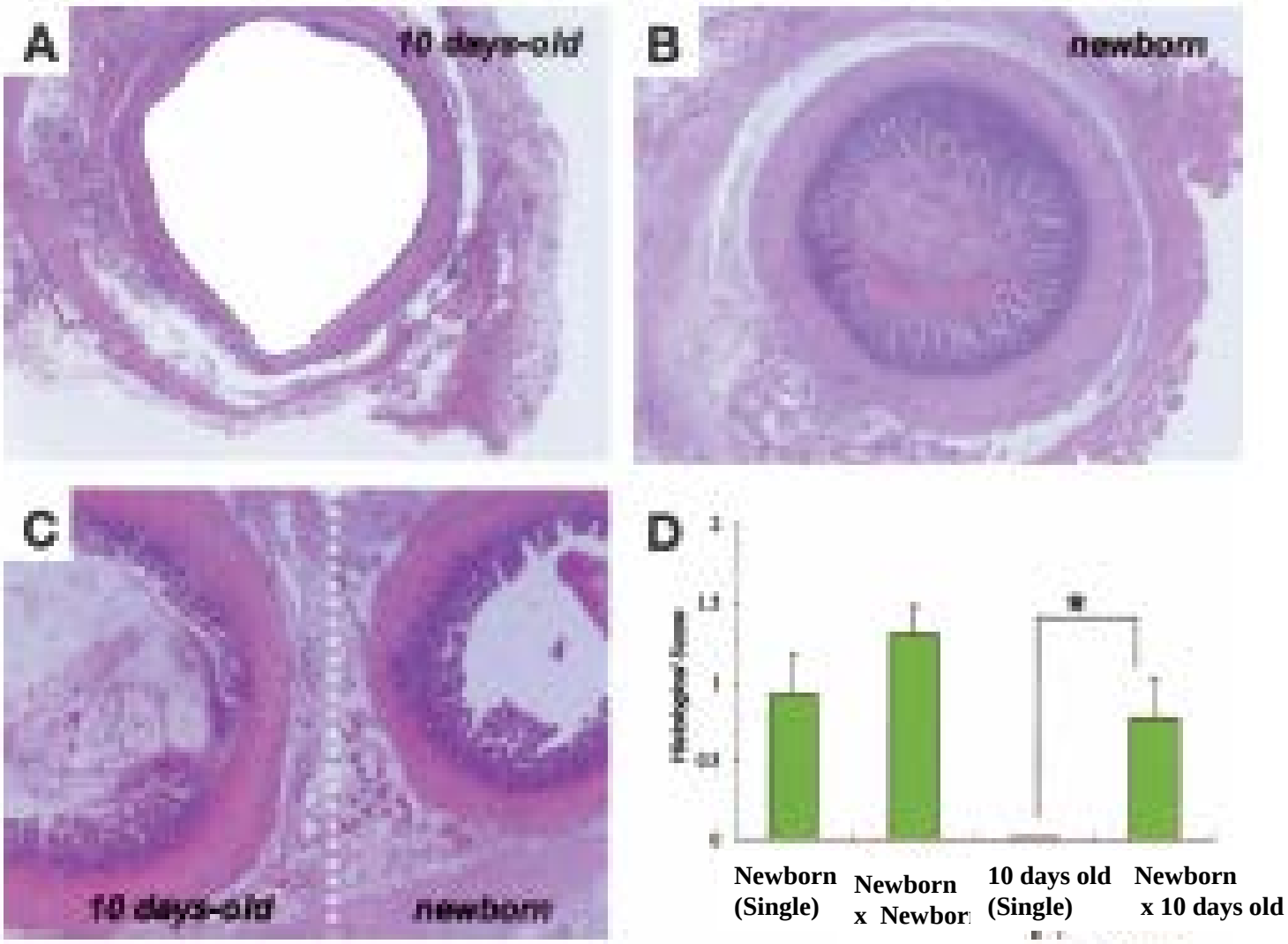

田原・小林　18ヒット

# Regeneration of the Rat Neonatal Intestine in Transplantation

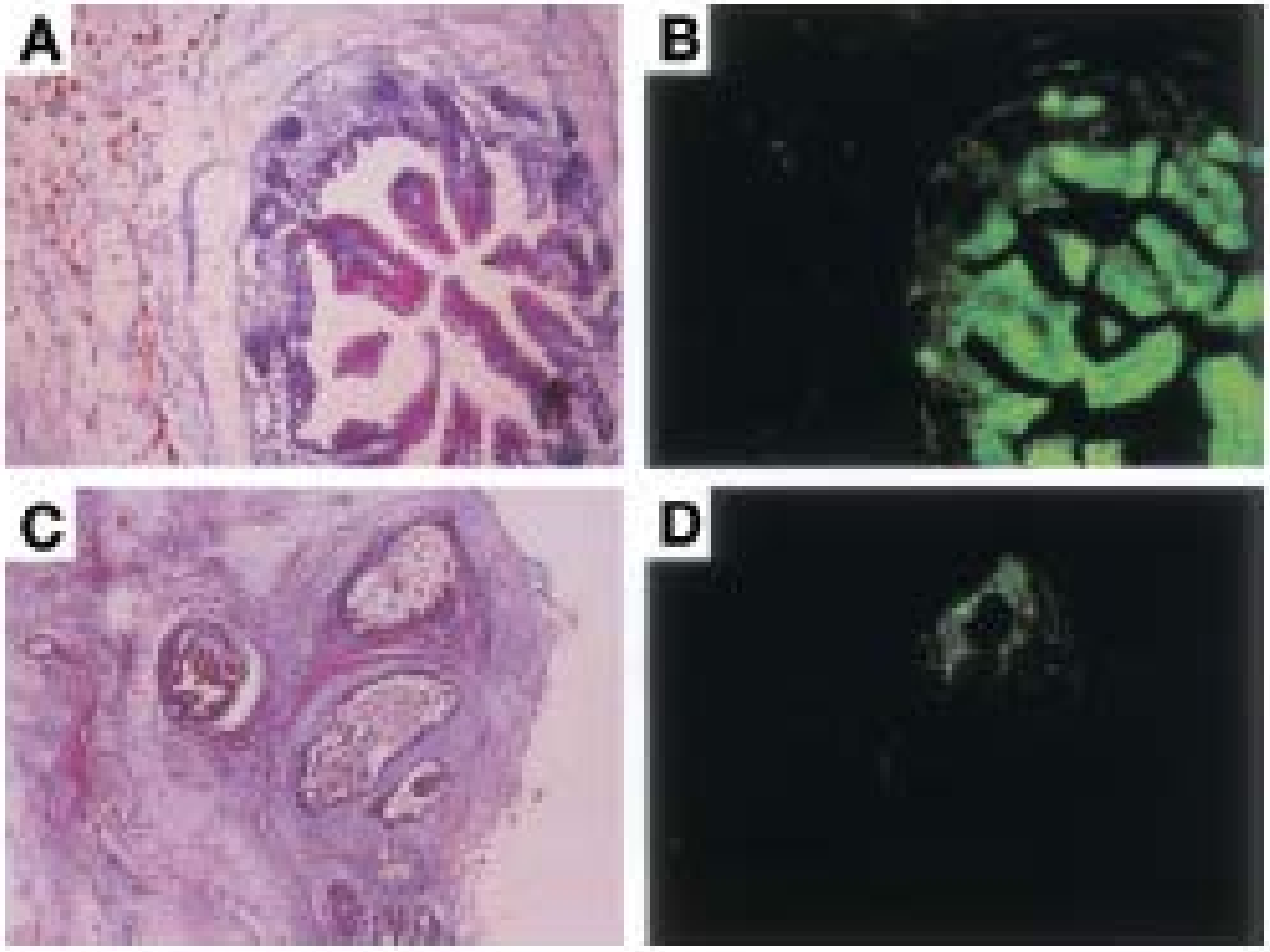



*( Tahara K, et al. Ann Surg 2005)*

# Maturation-incompetent 10-day-old intestinal graft was recovered in the presence of newborn graft.



# Histologic reconstitution of a 10-day-old graft from tissue aggregates.




*( Tahara K, et al. Ann Surg 2005)*

# 活性化した遺伝子

**TABLE 1.** Most Activated Transcripts in Regenerating 10-Day-Old Intestinal Grafts

| Gene Name | GeneBank | Ratio |
|---|---|---|
| B7.1 | AF010465 | 9.14 |
| SHPS-1 receptor-like protein with SH2 binding site | D85183 | 8.04 |
| Adenosine A2A receptor (ADORA2A) | S47609 | 7.73 |
| Cationic amino acid transporter 3 | AB000113 | 6.33 |
| Macrophage colony-stimulating factor I receptor (CSF1R) | X61479 | 5.51 |
| Nonprocessed neurexin III alpha | L14851 | 5.41 |
| Glycine transporter | M88595 | 5.12 |
| Protein kinase C delta type (PKC-delta; PRKCD; PKCD) | M18330 | 4.97 |
| Kidney oligopeptide transporter; peptide transporter 2 (PEPT2) | D63149 | 4.55 |
| Gastrin | M38653 | 4.55 |
| Transforming growth factor-beta receptor type II (TGF-beta receptor II) | L09653 | 4.48 |
| Synaptobrevin 2 (SYB2) | M24105 | 4.47 |
| Glutamate receptor subunit epsilon 3 (GRIN2C) | D13212 | 4.14 |
| Prostaglandin D2 receptor | U92289 | 4.12 |
| Glucose transporter 3 | U17978 | 4.11 |
| Somatostatin receptor 5 (SSTR5; SS5R) | L04535 | 4.01 |
| G protein-coupled receptor 27; gustatory receptor 27 (GUST27) | D12820 | 4 |

**TABLE 1.** Most Activated Transcripts in Regenerating 10-Day-Old Intestinal Grafts

| Gene Name | GeneBank | Ratio |
|---|---|---|
| *N*-Methyl-D-aspartate receptor-2A subunit (NMDAR2A) | AF001423 | 3.97 |
| Retinoid X receptor-alpha (RXR-alpha; RXRA) | L06482 | 3.93 |
| Mitogen-activated protein kinase 9 (MAPK9) | L27112 | 3.92 |
| Mitogen-activated protein kinase 5 (MAPK5) | U37462 | 3.84 |
| Liver Na+/Cl− betaine/GABA transporter | U28927 | 3.74 |
| Cyclin G-associated kinase (GAK) | D38560 | 3.71 |
| Sodium channel SCNB2, beta 2 subunit, brain | U37026 | 3.63 |
| Insulin-like growth factor binding protein 5 (IGF-binding protein 5; IGFBP5) | M62781 | 3.62 |
| Voltage-dependent L-type calcium channel alpha 1C subunit (CACNA1) | M59786 | 3.53 |
| Voltage-gated dihydropyridine-sensitive L-type calcium channel beta 3 subunit | M88751 | 3.52 |
| ADP-ribosylation factor 2 | L12381 | 3.51 |
| Retinoid X receptor beta (RXR-beta; RXRB) | M81766 | 3.4 |
| cAMP-dependent protein kinase type I alpha regulatory subunit (PRKAR1A) | M17086 | 3.3 |
| Cytochrome P450 IIA1 (CYP2A1) | J02669 | 3.28 |
| Mineralocorticoid receptor (MCR) | M36074 | 3.18 |
| Sodium/potassium-transporting ATPase alpha 2 subunit (Na+/K+ ATPase; ATP1A2) | M14512 | 3.15 |
| ATPase, subunit F, vacuolar (vatf) | U43175 | 3.15 |
| Aquaporin 5 (AQP5) | U16245 | 3.07 |
| G protein, gamma 5 subunit | M95780 | 3.03 |
| Proteasome subunit RC10-II | D21800 | 3.01 |

*( Tahara K, et al. Ann Surg 2005)*

# 発現低下した遺伝子

**TABLE 2.** Down-Regulated Genes In Regenerating 10-Day-Old Intestinal Grafts

| Gene Name | GeneBank | Ratio |
|---|---|---|
| Apolipoprotein AIV (APOA4; APOC4) | M00002 | 0.08 |
| Glutamic acid decarboxylase (GAD65) | M72422 | 0.13 |
| Glucose-6-phosphate dehydrogenase | X07467 | 0.15 |
| Insulin-like growth factor binding protein, complex acid-labile subunit | S46785 | 0.17 |
| Intestinal fatty acid-binding protein (I-FABP; FABPI) | M35992 | 0.18 |
| Apolipoprotein AI (APOA1) | M00001 | 0.19 |
| Sodium/chloride neurotransmitter transporter | S68944 | 0.22 |
| Cathepsin L | Y00697 | 0.23 |
| Mitochondrial hydroxymethylglutaryl-CoA lyase (HMG-CoA lyase) | Y10054 | 0.24 |

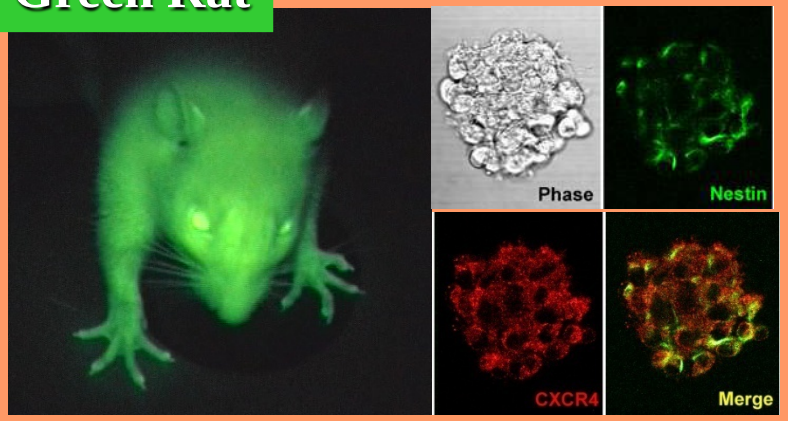
**TABLE 2.** Down-Regulated Genes In Regenerating 10-Day-Old Intestinal Grafts

| Gene Name | GeneBank | Ratio |
|---|---|---|
| Serum/glucocorticoid-regulated serine/threonine protein kinase (SGK) | L01624 | 0.24 |
| Interleukin 2 receptor-alpha subunit (IL2R- alpha; IL2RA) | M55049 | 0.25 |
| Prolactin-like protein A (rPLP-A) | M13750 | 0.25 |
| p55CDC; cell division control protein 20 | U05341 | 0.26 |
| Myelin proteolipid protein (PLP); lipophilin; DM20 | M11185 | 0.26 |
| Set beta isoform + Set alpha isoform; neural plasticity-related protein | S68987 | 0.26 |
| Liver long chain fatty acid-CoA ligase (FACL2) | D90109 | 0.3 |
| Activin receptor type I (ACVR1; ACTR1) | L19341 | 0.31 |
| Gamma-aminobutyric acid (GABA) receptor beta 1 subunit | X15466 | 0.31 |
| Syntaxin 3 (STX3) | L20820 | 0.32 |

*( Tahara K, et al. Ann Surg 2005)*

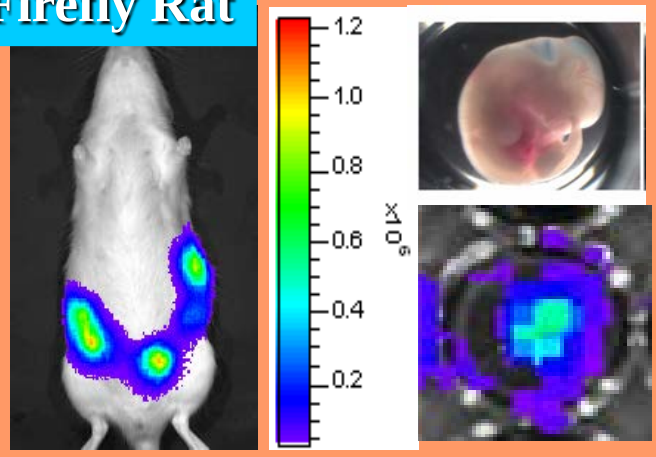
# Powerful Tool for Translational Research

## Green Rat



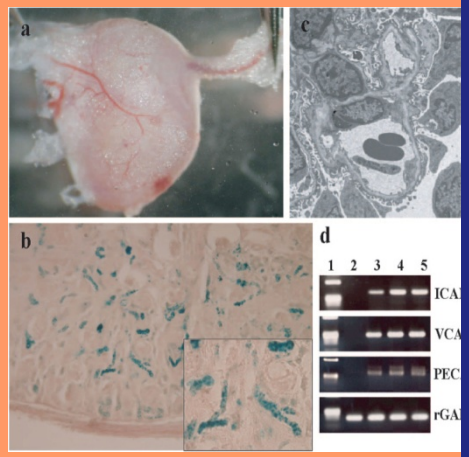

*Neuroscience*

## Firefly Rat




*In vivo bioimaging*

## Blue Rat




*Development*


## Red Rat


*Gene Therapy*

# 世界を駆けるＴｇラット


**Germany**
*EK Geissler(Regensburg)*
*G Nikkhah (Freiburg)*
*R Tolba (Bonn)*





**Canada**
*A Keating (Toronto Univ)*

**U.S.A**
*John Critser (Missouri Univ)*
*SS Thorgeirsson (NCI)*
*P Leone(RWJ Med Sch)*


**Thailand**
*A Sereemaspun*
**Singapore**
*DW Hutmacher*
*S Cool (Bioporis)*

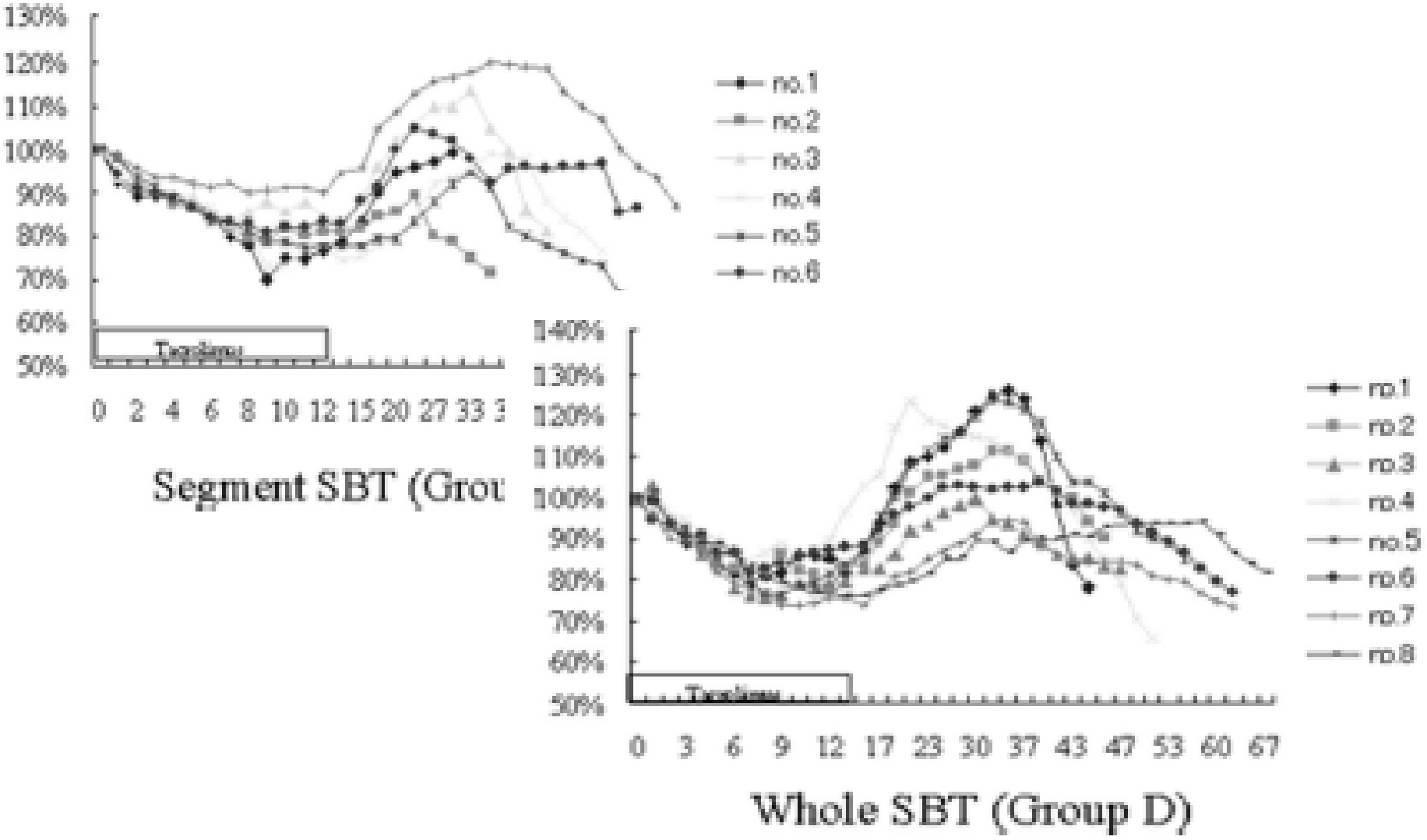

**Australia**
*GA Bishop (Sydney)*


2004年12月
カフ准教授
ミノール教授
トルバ先生
ヒルナー教授
当時留学中の田原先生
（東大小児外科）
レーゲンスブルグ留学予定
の井上先生（筑波小児外科）


2007年6月
ボン留学中の藤代先生
トルバ先生
秦先生
（京大・移植外科）
藤代先生
（東大・小児外科）
VISIO

# *Immnologic benefits of longer graft in rat allogenic small bowel transplantation*

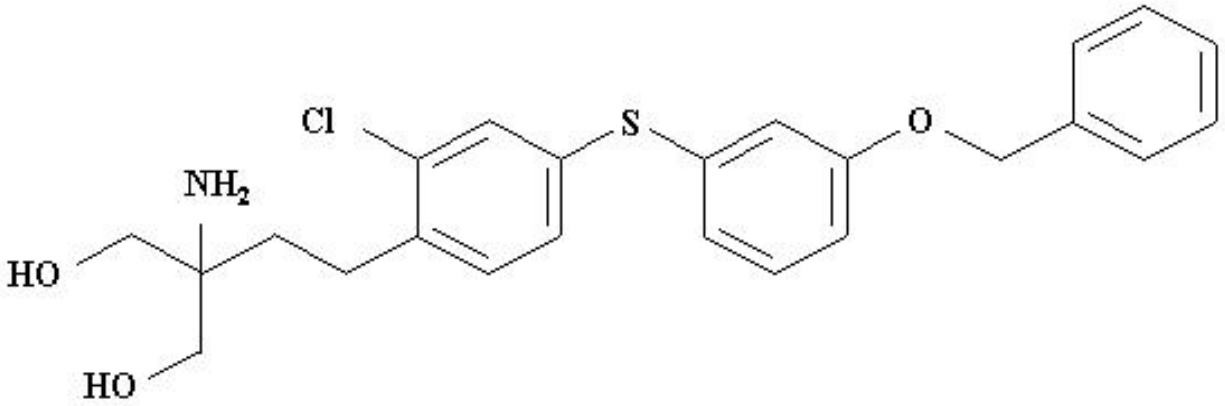
藤代・小林　12ヒット



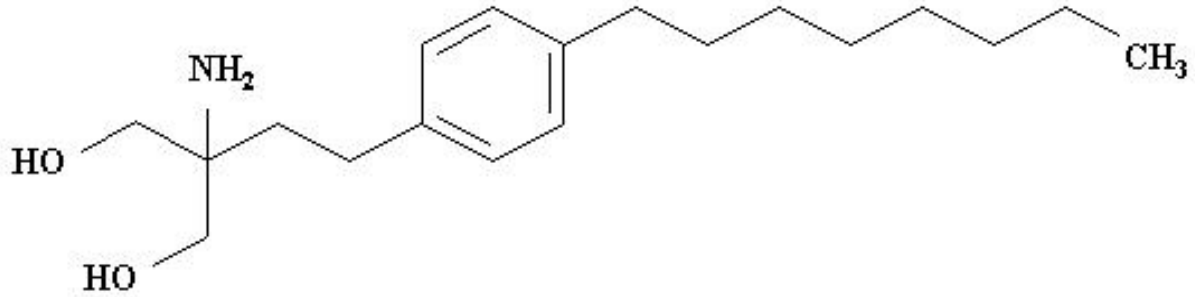

*(Fujishiro J, et al, Transplantation 2005 )*

# Comparison of Molecular structure of KRP-203 with FTY720

KRP-203



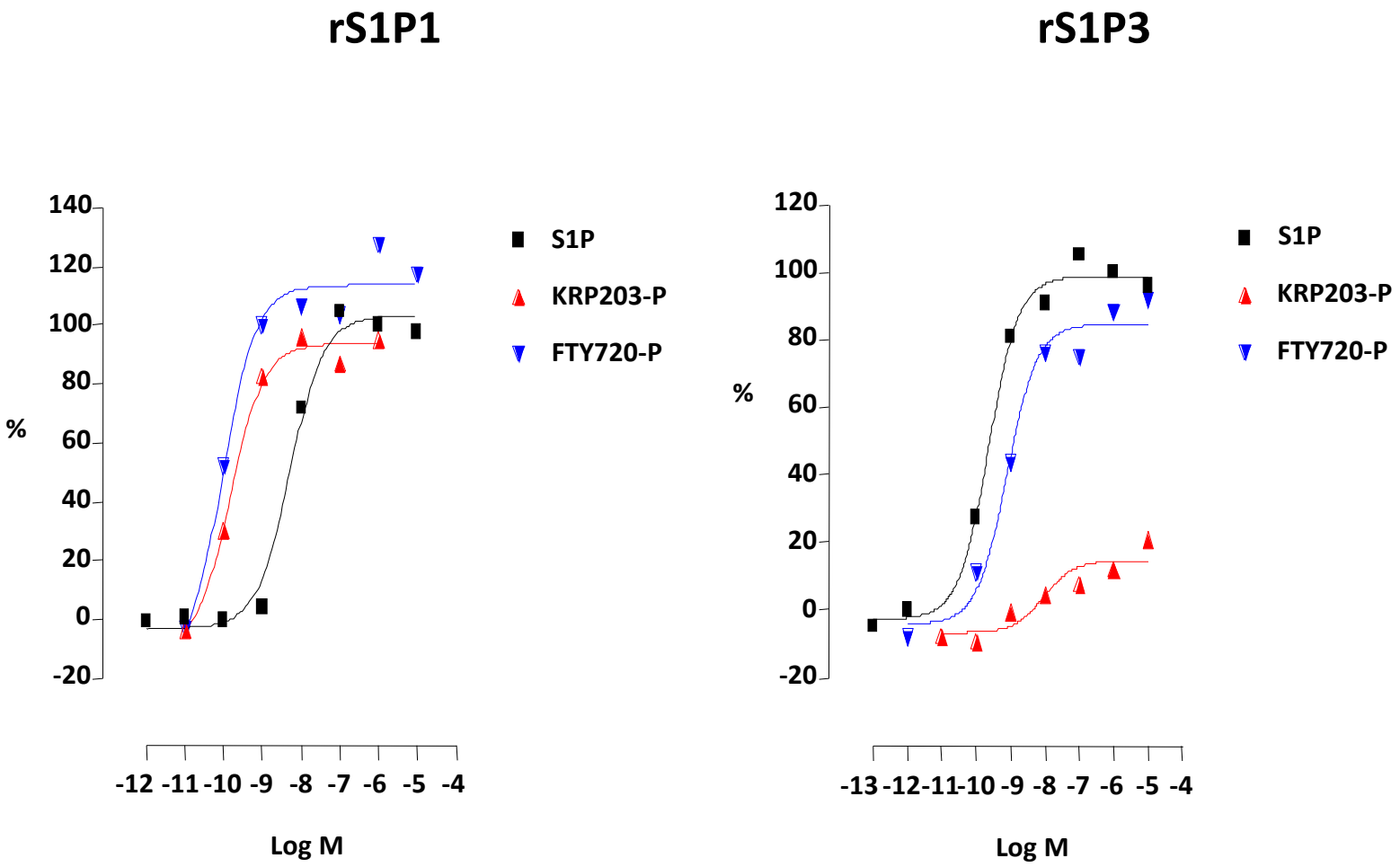

FTY720




JICHI MEDICAL SCHOOL

KYORIN

# KRP-203-P highly activates Rat $S1P_1$, but less $S1P_3$




Calcium Mobilization Assay in the Rat $S1P_1$ or $S1P_3$-transduced CHO-K1 cells.

*(Shimizu, et al. Circulation 111;222,2005)*

Lists of publication of a novel **S**phingosin-**1**-**p**hosphate receptor agonist, **KRP-203**


*1. Shimizu H, et al. Circulation 111;222,2005*

*2. Takahashi M, et al. Transplant Proc 37;143,2005*

*3. Suzuki C, et al. J Heart Lung Transplant 25;302,2006*

*4. Fujishiro J, et al. J Heart Lung Transplant 25;825,2006*

*5. Fujishiro J, et al. Transplantation 82;804, 2006*

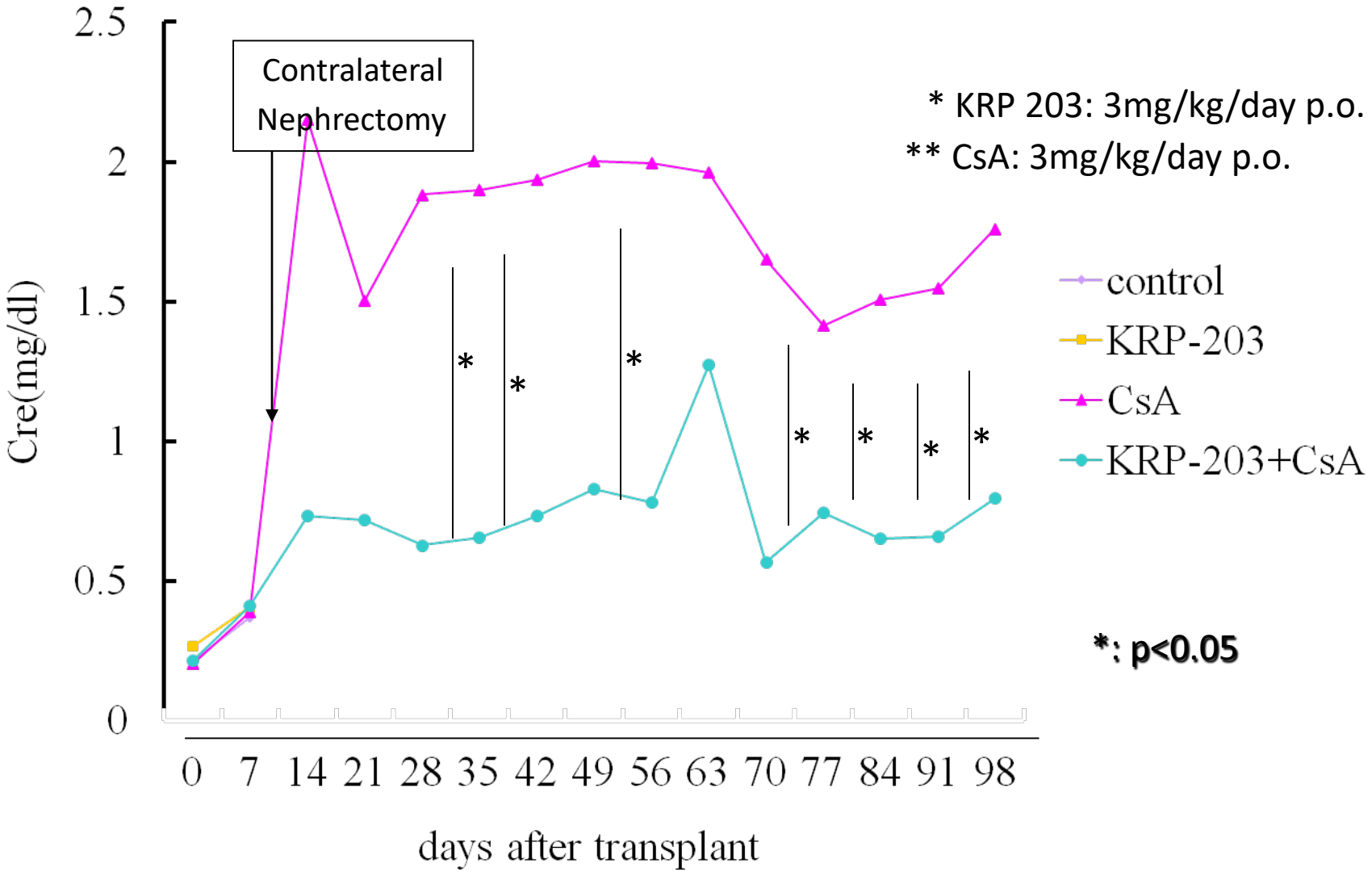
*6. Kaneko T, et al. Biochem Biophys Res Commun 345;85,2006*

*7. Ogawa R, et al. Biochem Biophys Res Commun 361;621,2007*


JICHI MEDICAL SCHOOL

KYORIN

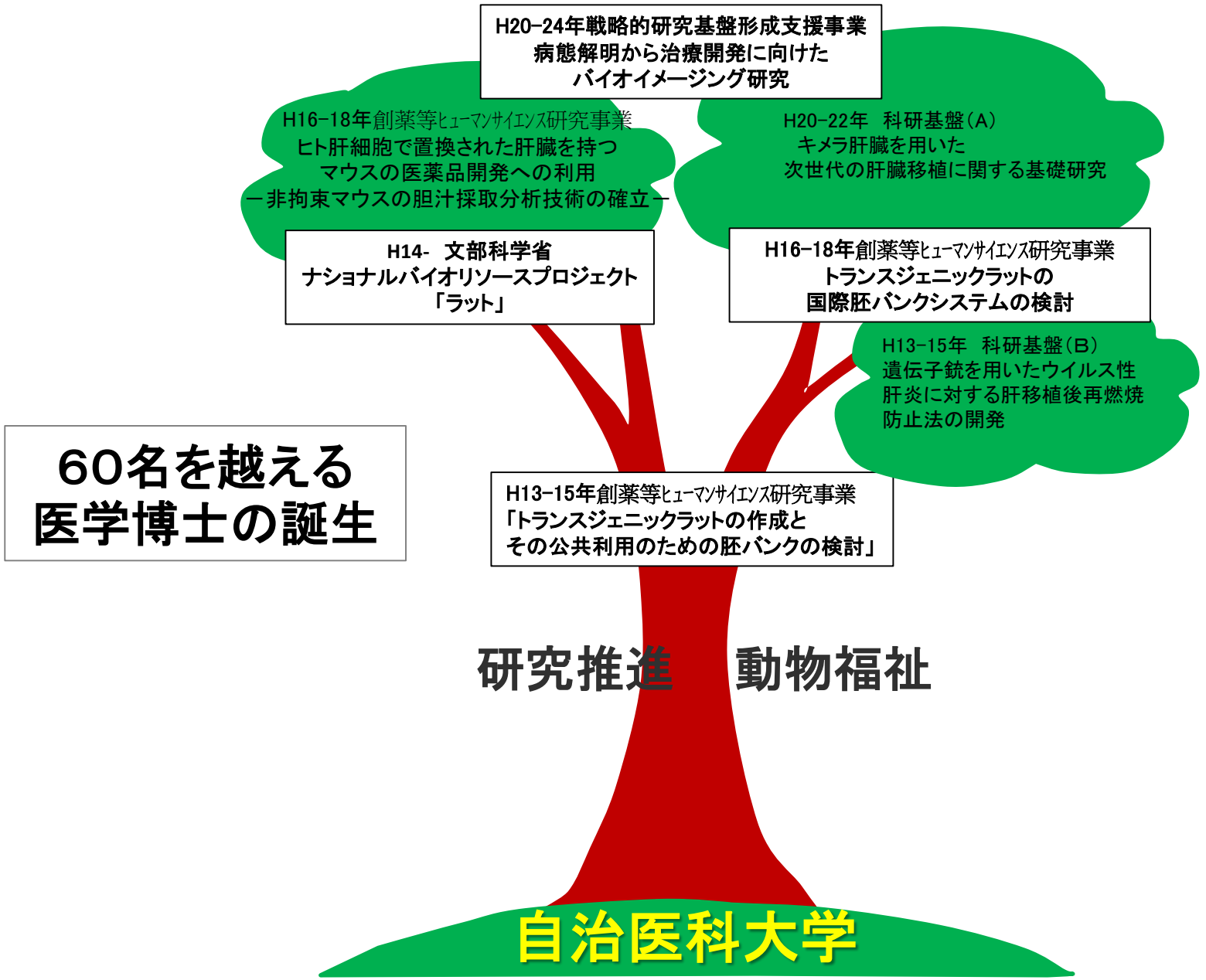
# Abrogation of Renal Allograft Rejection by KRP-203 with subtherapeutic dose of Cyclosporine A




*(Fujishiro J, et al. Transplantation 2006)*

「家族に嘘をつく！」

# バイオイメージング技術を導入した実験動物モデルの展開




**60名を越える**
**医学博士の誕生**

# 自治医科大学　先端医療技術開発センター　　沿革

**2001年**　栃木県重点分野研究開発促進事業（医療福祉関連）採択。「医療技術 トレーニングシステムの構築」をテーマに保健所からの譲渡犬を用いた動物実験 を全て中止し、ブタの実験使用推進を開始。

**2007年04月**　自治医科大学実験医学センター内に「医療技術トレーニング部門」設置

**2008年**　文部科学省
「私立大学戦略的研究基盤形成支援事業」
の一つとして、自治医科大学の「大型動物（ミニブタ）を用いた先進的医療技術実現化」事業が採択

**2009年04月**
先端医療技術開発センター(CDAMTec)開設

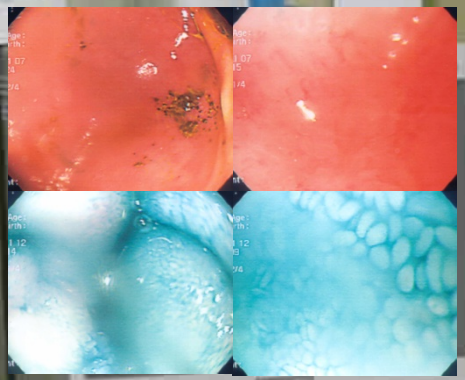
（自治大ホームページより）

# レギュラトリー・サイアンスのシステムを導入と運営ノーハウの蓄積

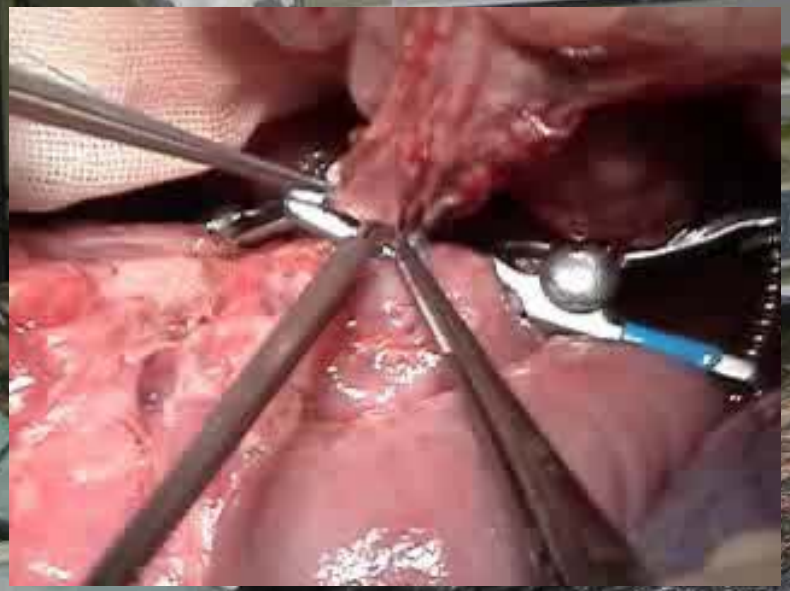



# Assessment equally to clinical procedure

吉野・小林　12ヒット

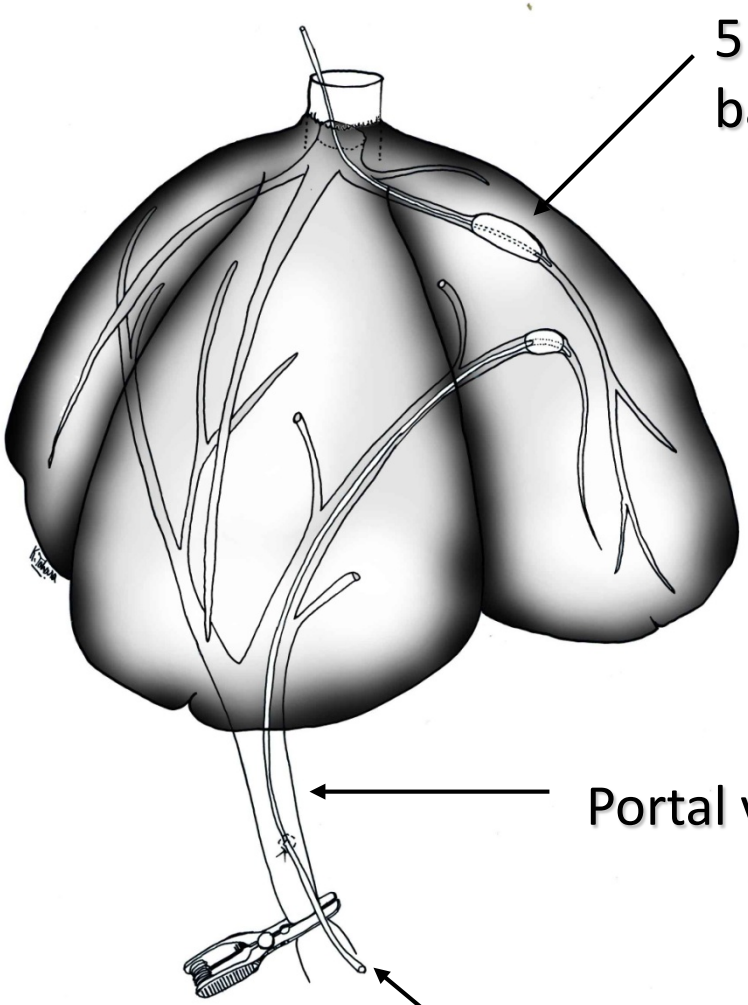


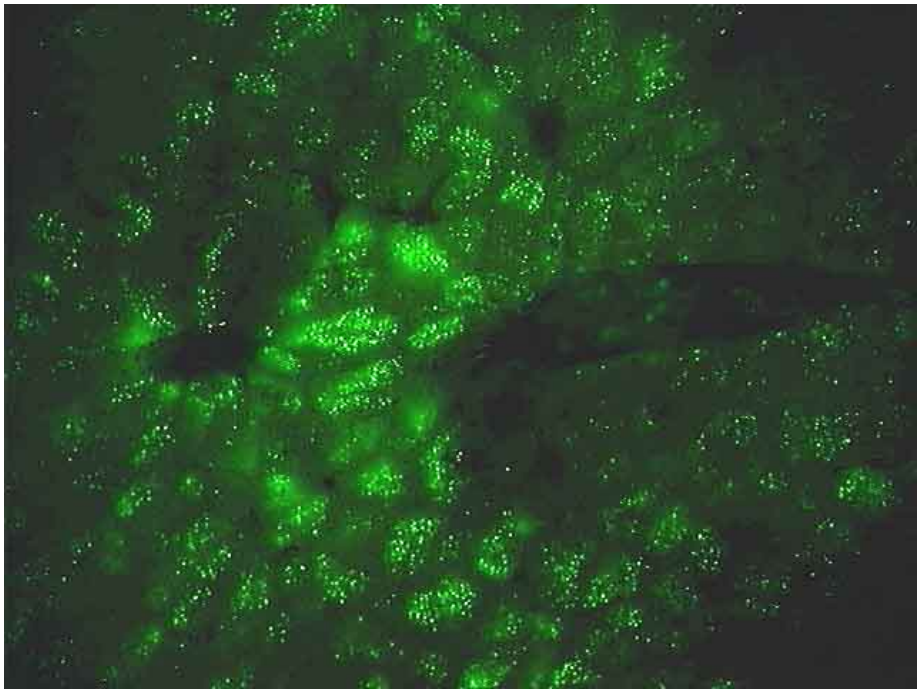
・Zoom Scoop



(Yoshino H, et al. Transplantation 76;442,2003)

# *Naked plasmid DNA transfer to the porcine liver*

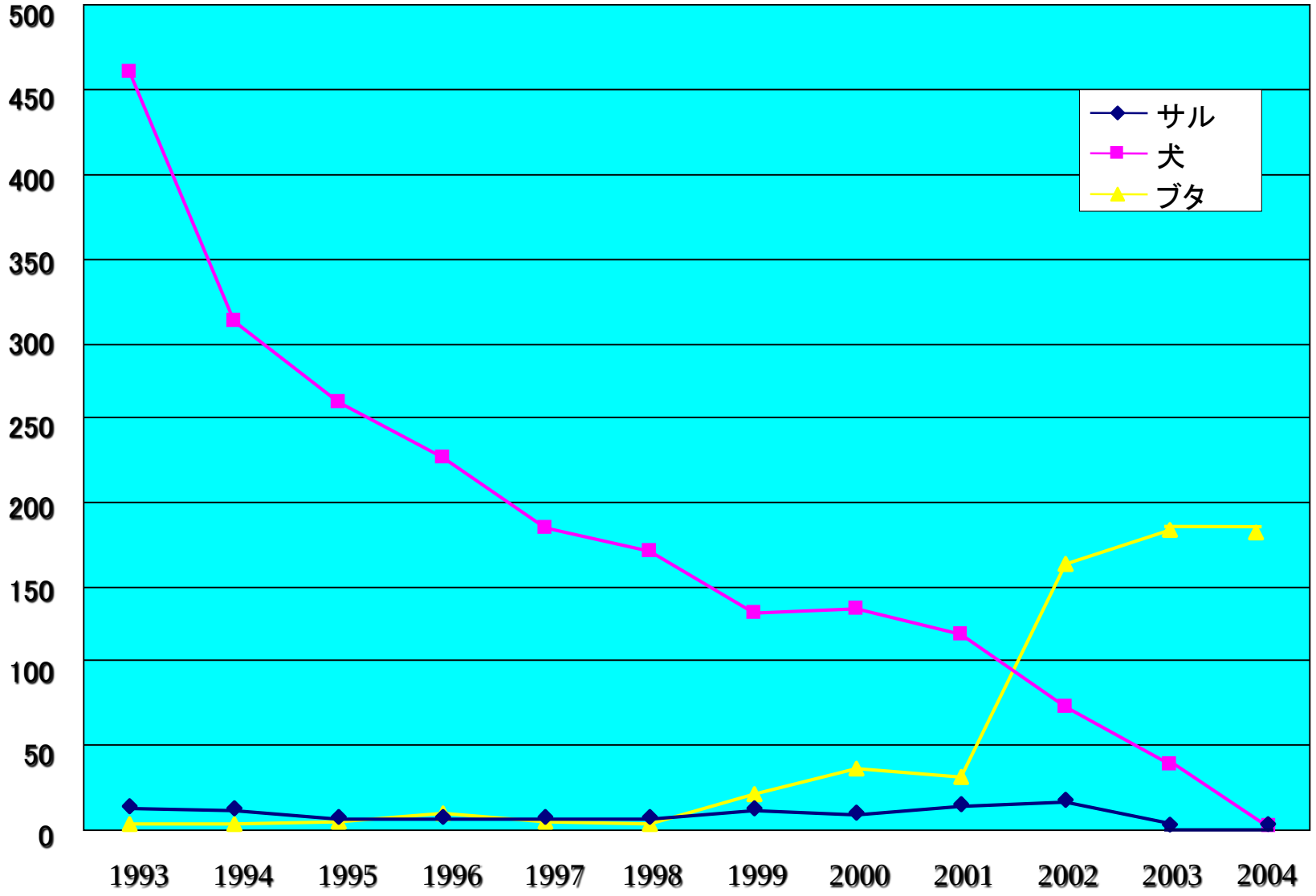


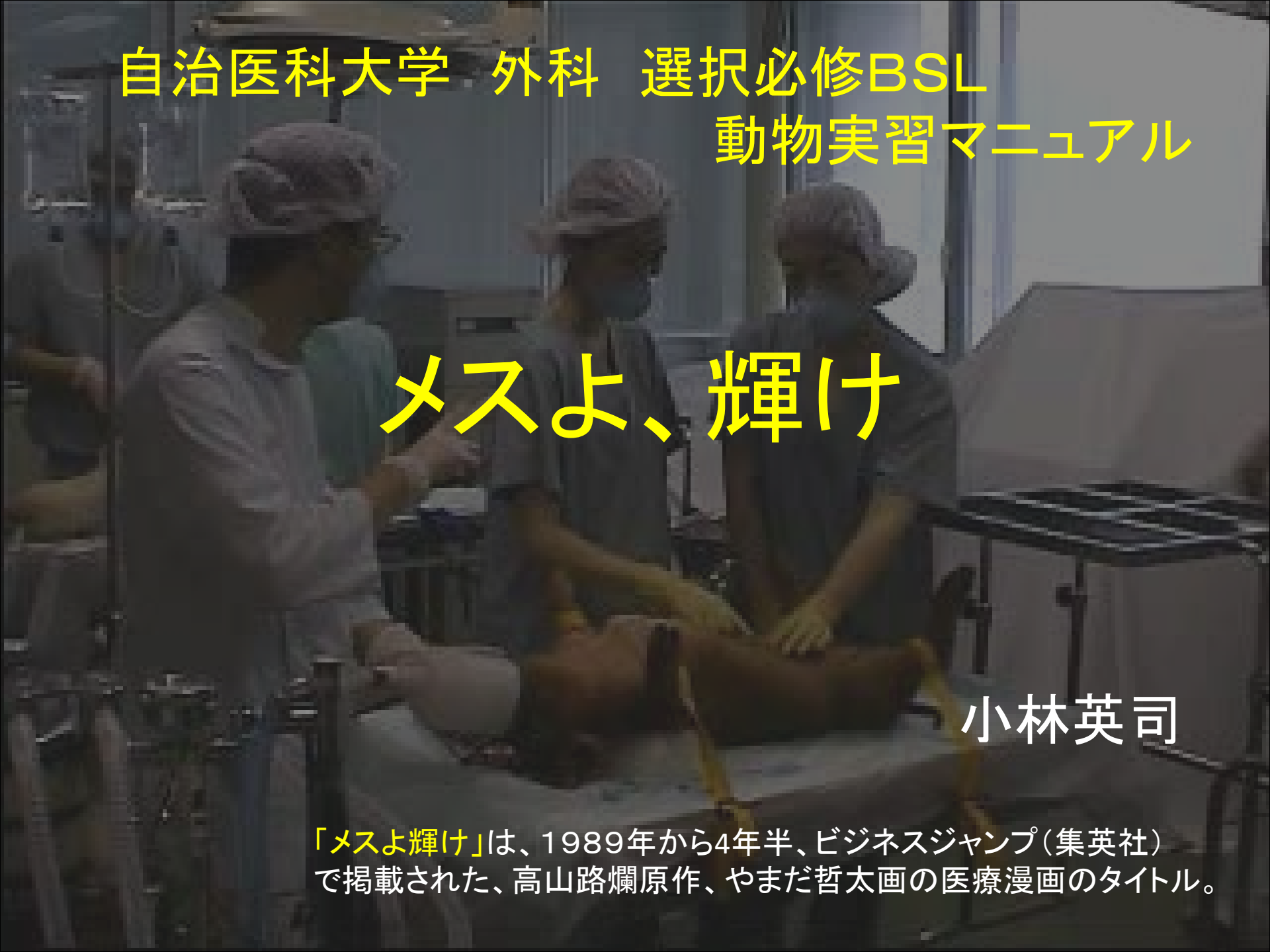



*(Yoshino H, et al. Gene Therapy 2006)*

「パートナーですから！」

# 自治医科大における大型実験動物の推移





自治医科大学　外科　選択必修BSL
動物実習マニュアル

# メスよ、輝け

小林英司

「メスよ輝け」は、1989年から4年半、ビジネスジャンプ（集英社）で掲載された、高山路爛原作、やまだ哲太画の医療漫画のタイトル。

# ATOM Course from 2008

## As the first Institute for Asia

COMMITTEE ON TRAUMA

NEWS

MARCH/APRIL 2012

EVENTS

- Point/Counterpoint Acute Care Surgery Conference Coming Soon
- Update on ATOM–Japan
- COT and MASSMAC Sign MOU
- Level IV Status Developed
- PHTLS Signing Ceremony Held in Lebanon

MEETINGS

- COT Annual Meeting
- ATLS Region Meeting Held in UAE
- Upcoming Region Meetings

FYI

- Q&A with Dennis Ashley, MD, FACS, Information Technology Committee Chair
- New Committee on Trauma Member Appointed
- New Appointees to the Regional Committees on Trauma
- TQIP Update
- NTDB Call for Data

PRODUCTS

- New COT Merchandise Available

THANK YOU

- A. Lee Dimick, MD, FACS
- Eric Kennedy, MD, FACS

ABOUT OUR ORGANIZATION

EVENTS

### Point/Counterpoint Acute Care Surgery Conference Coming Soon

The 31st annual Point/Counterpoint Acute Care Surgery Conference will be held June 15–18 at the Gaylord National Hotel and Convention Center in National Harbor, Maryland. Please visit www.pointcounterpoint.com to register and to obtain more information on the meeting.

### Update on ATOM–Japan

by Alan Tyler, MD

Since the 2008 promulgation of ATOM in Japan, we have held 11 courses, trained 27 instructors, and enrolled more than 50 surgeons. The program has grown slowly and steadily, allowing us to assure a quality international program. Presently, there are four active ATOM sites covering all of Japan, including Tohoku University, Jichi Medical University, Osaka City University, and Ryukyu University.

The newest course site, MUDOLO, is located in Kobe City near Osaka at a Bio-Tech incubator zone, which was rebuilt after the tragic Great Hanshin earthquake of 1995 (magnitude 7.2). This site is shared by many organizations and serves as an outstanding venue for ATOM courses. We look forward to the next course, which will be held in November 2012.

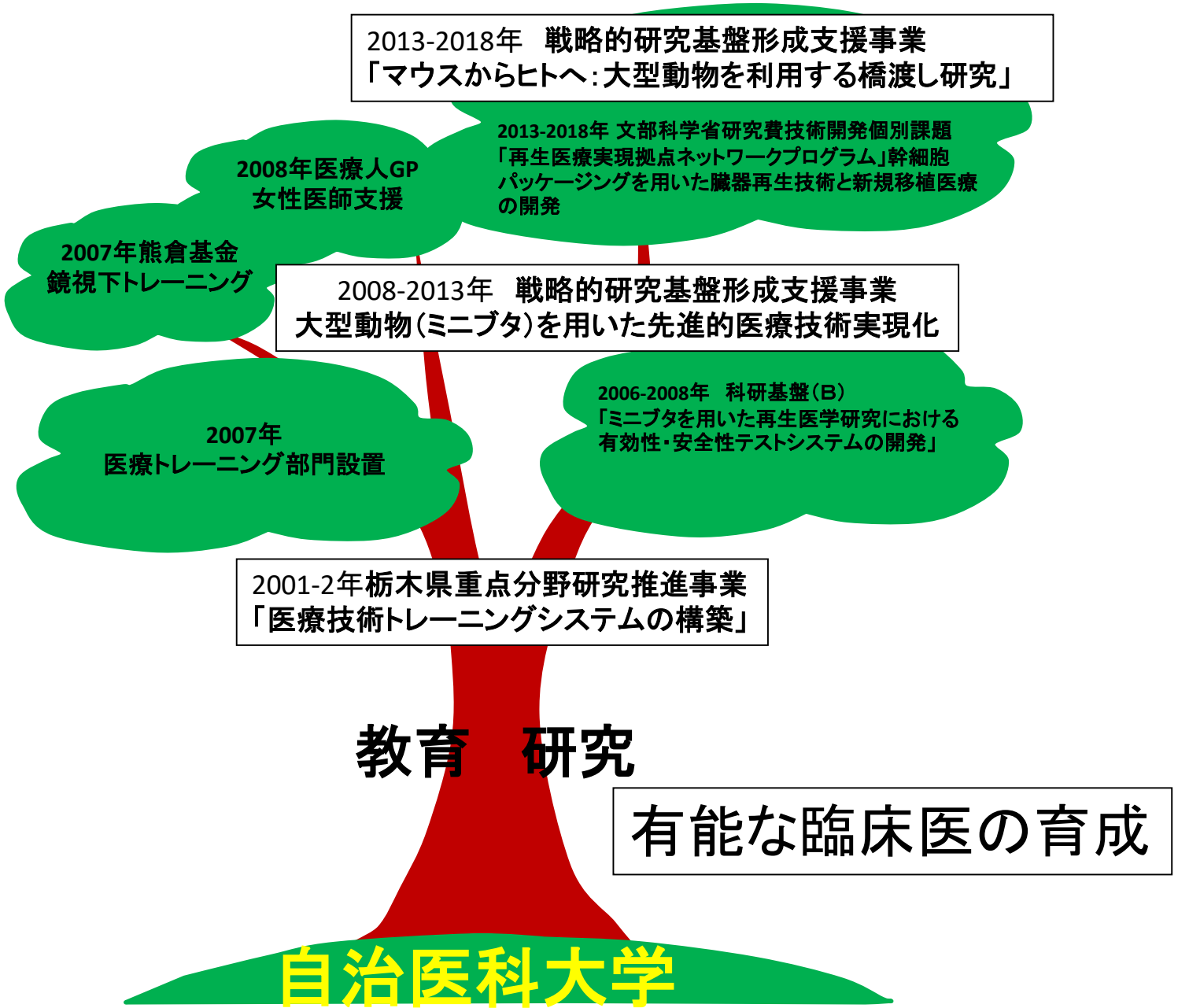


Beautiful new instruments shelved among ATOM–Japan sites. The inscription reads "ATOM—Tenchi, University Hospital."



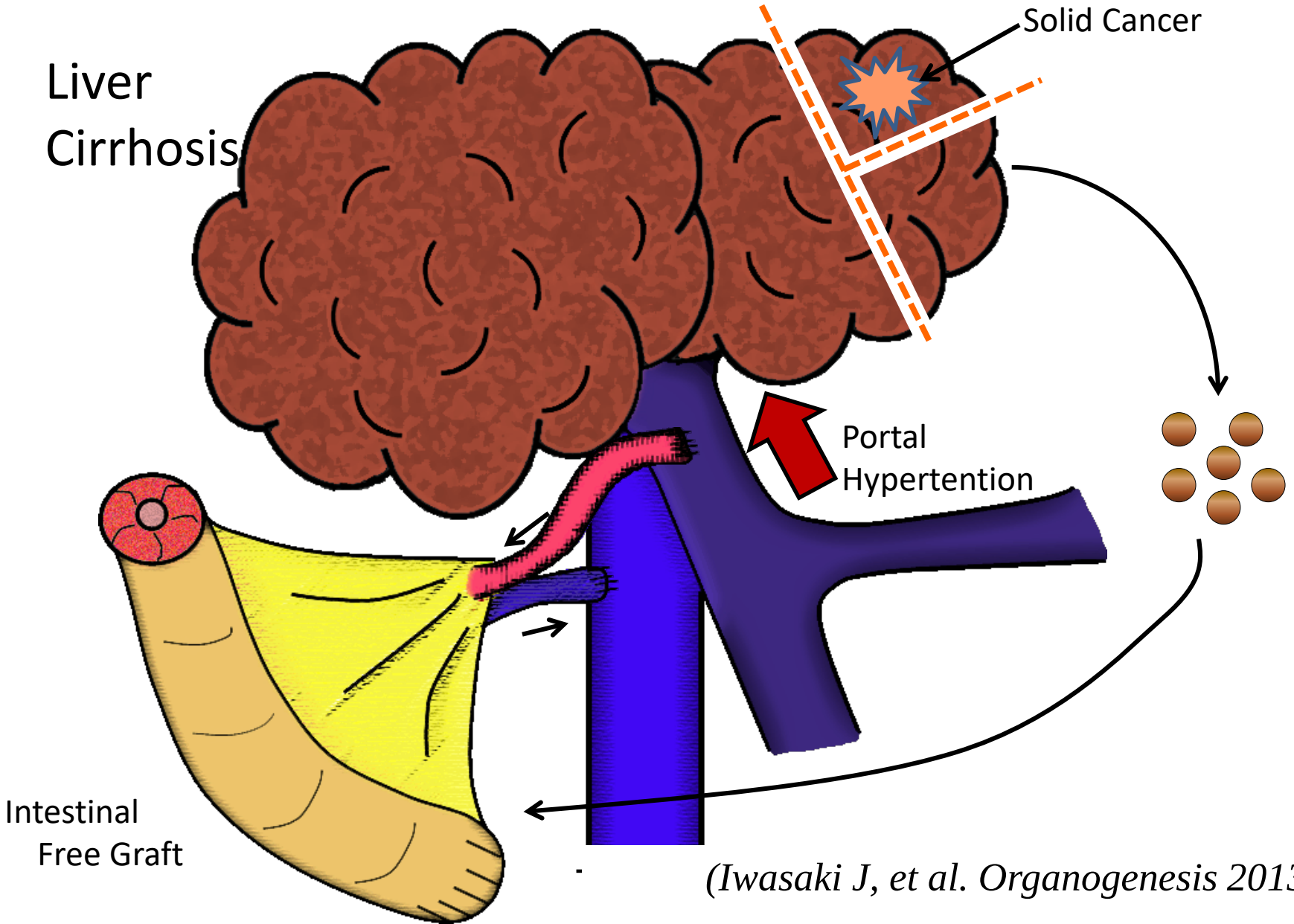
The ATOM–Japan group after the first ATOM course in Japan in December 2008.

# 世界一の実験専用ブタシステムの構築



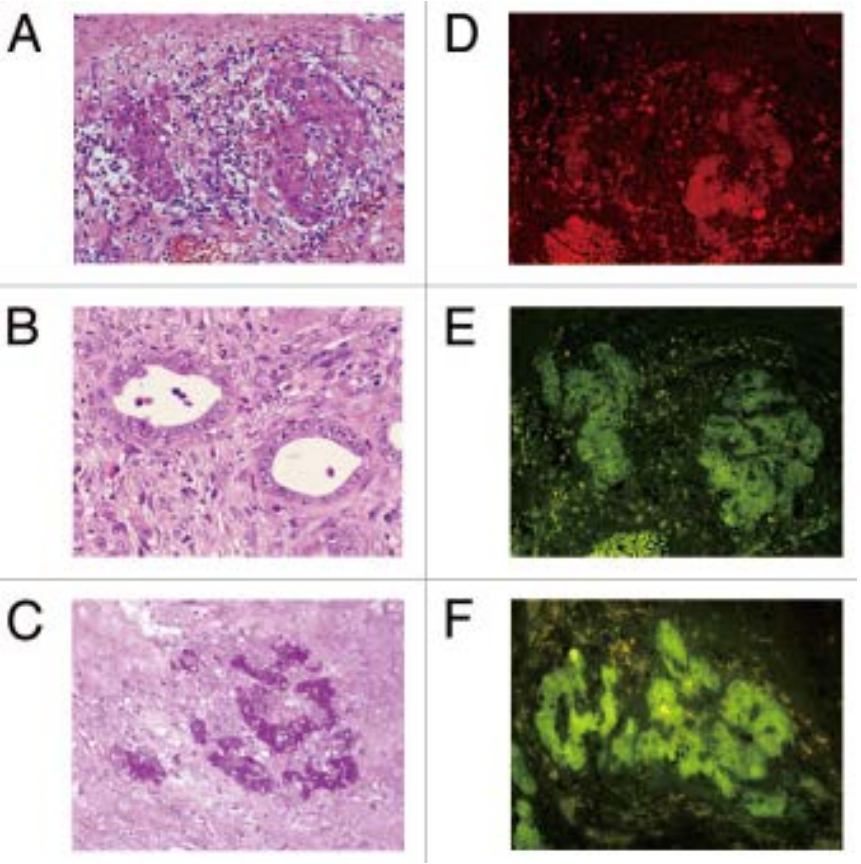
「惑わすような論文
は書けません！」

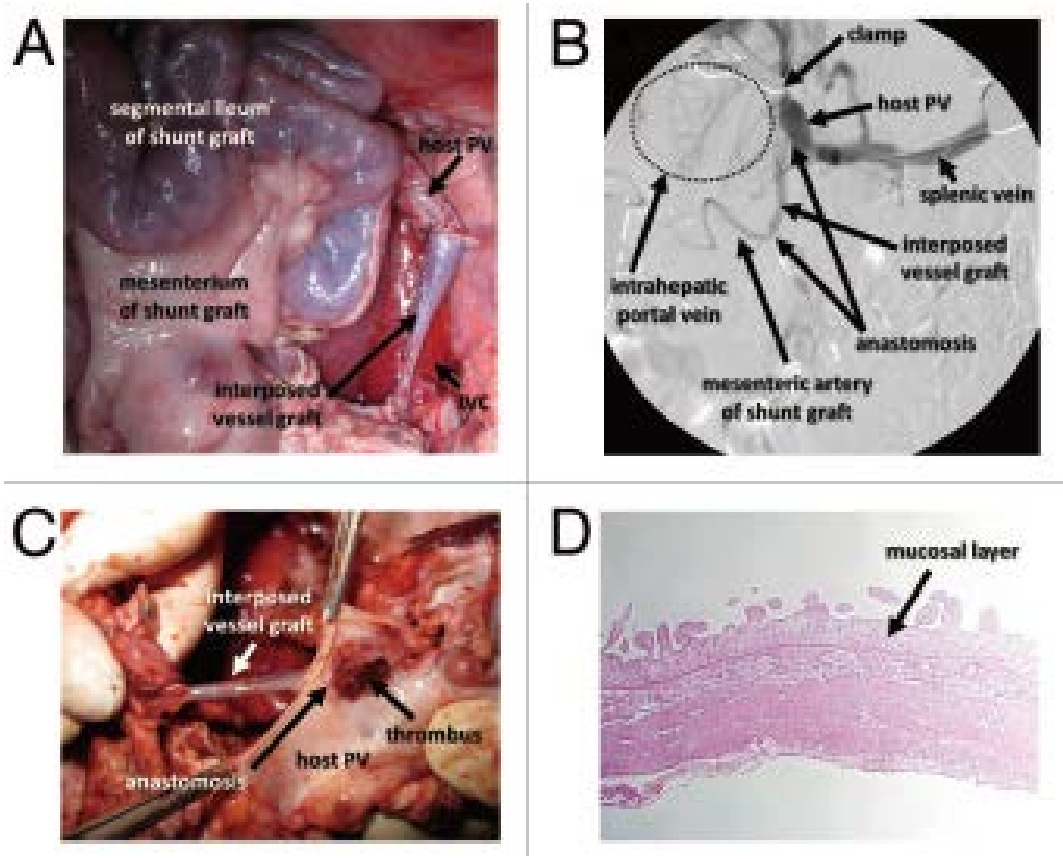
# Portocaval shunt for hepatocyte package: Challenging application of small intestinal graft in animal models




*(Iwasaki J, et al. Organogenesis 2013)*

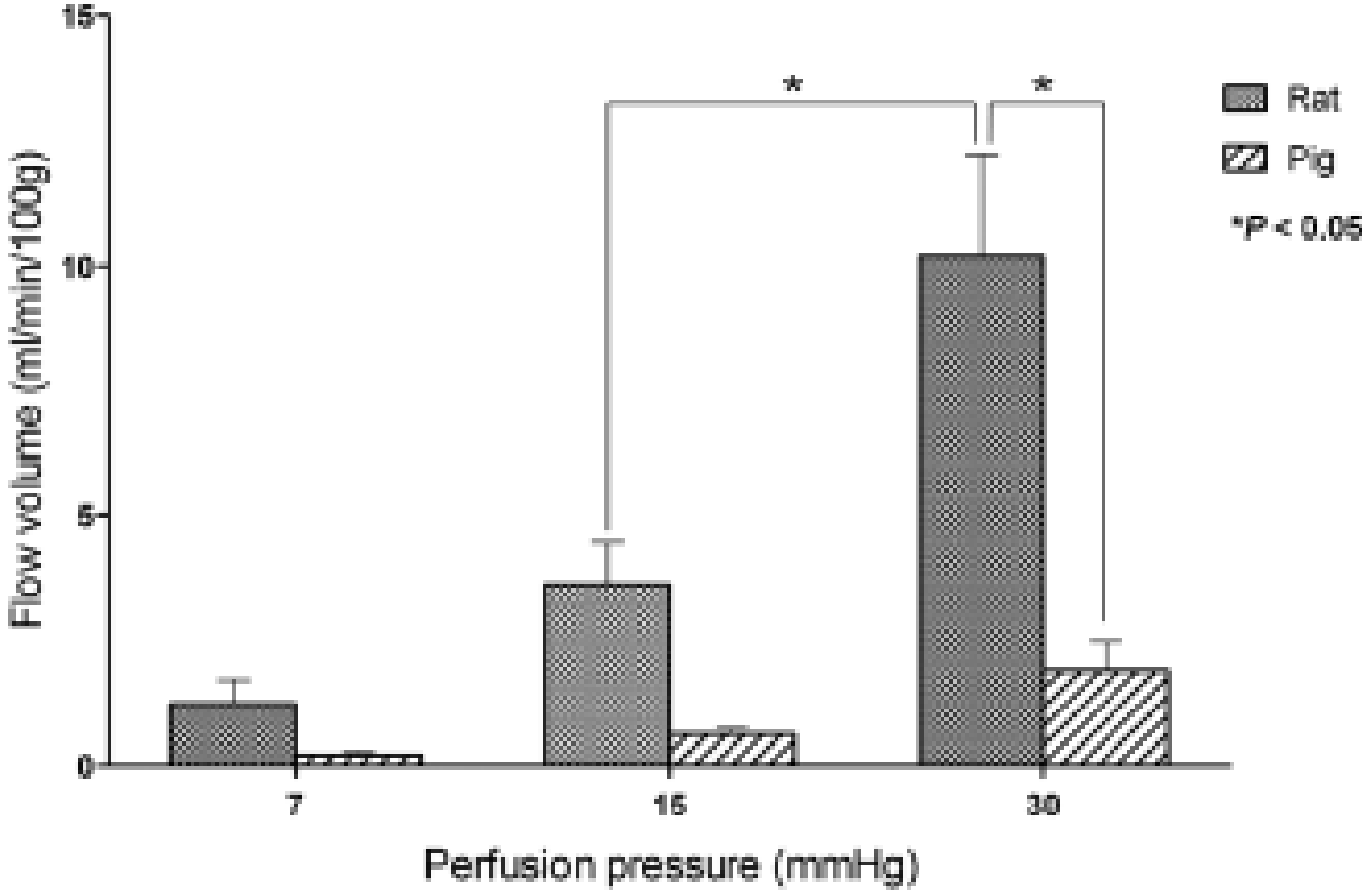
# Hepatocyte Cluster was observed in the submucosa of normal intestine, but not in the shunted intestinal graft




*(Iwasaki J, et al. Organogenesis 2013)*

# Relationship between flow volume and perfusion pressure in whole intestine ex vivo in rats and pigs.



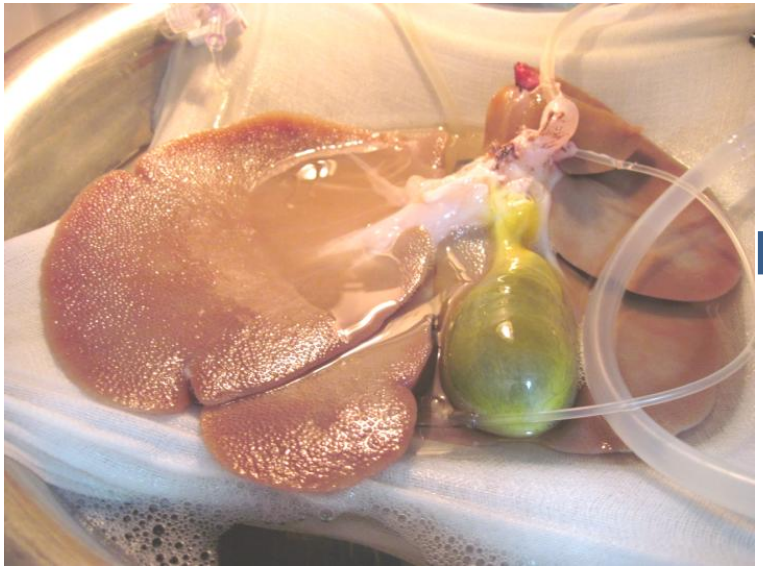

*(Iwasaki J, et al. Organogenesis 2013)*

# Production of three-dimensional whole-organ scaffolds by perfusion-decellularizatoin technology

| Organ | Proof-of-concept rodent model | Pig model |
|---|---|---|
| Heart | *(Ott HC et al. Nature Med 2008)* *(Lu TY et al. Nature Com 2013)* | |
| Kidney | *(Ross EA et al. JASN 2009)* *(Song J, et al. Nature Med 2013 )* | *(Orlando G et al. Ann Surg 2012)* |
| Lung | *(Ott HC et al. Nature Med 2010)* | *(Gilpin SE, et al. J Heart Lung Transplant 2014)* |
| Liver | *(Uygun BE et al.Nature Med 2010)* | *(Yagi H et al. Cell Transplant 2013)* |

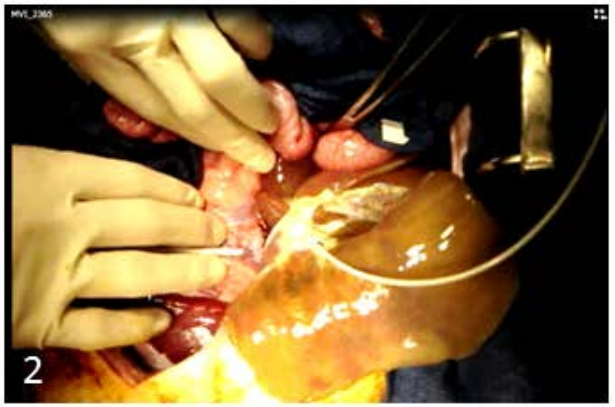
*(**Table** modified from Hata T, et al. Organogenesis 2013)*

# Decellularization of the porcine Liver

*(Teratani T, et al. JSRM2013 )*

# Transplantation of the creating liver

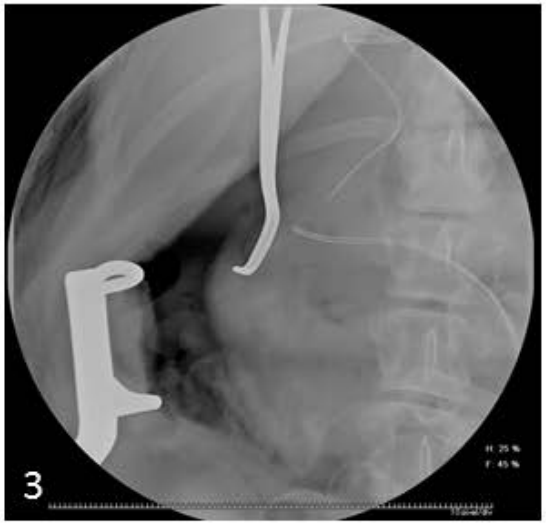




*(Urahashi T, et al. JSS 2013 & 2014 )*

# Assessment of the Graft Liver






*(Urahashi T, et al. JSS 2013 & 2014 )*

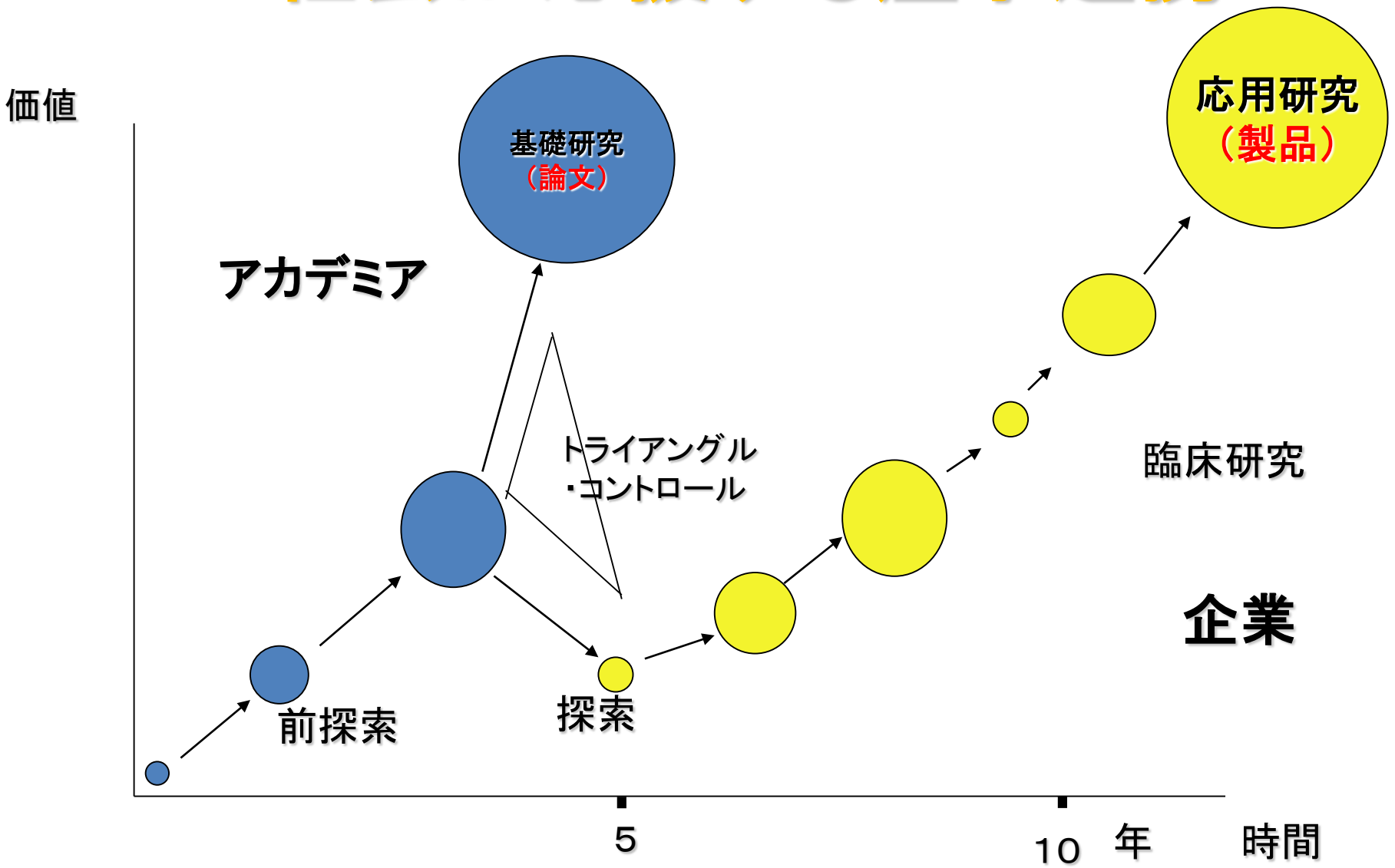
# 2014年　これからやりたいこと

# 臓器再生医学の展開
# Organ Fabrication

## 「自我作古」

「我より古を作す（われよりいにしえをなす）」と訓み、前人未踏の新しい分野に挑戦し、たとえ困難や試練が待ち受けていても、それに耐えて開拓に当たるという、勇気と使命感を表した言葉。

# 社会が応援する産学連携




科学技術未来戦略ワークショップ資料（小林；2010年3月8日、東京）より改編

# 変わらぬ心

ヒューマニズムは、外科学の進路をまっすぐに維持するただ一つの原動力である。

ヒューマニズムこそ、我々外科医に対して権利の限界と義務の範囲を示してくれる教理である。

This is a passage from the book
“La Philosophie de la Chirurgie” (1951),
by the great French surgeon René Leriche.