Why doctors are in need of pushing forward researches?

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The reason why doctors need to continue researches

Basic Research

Translation (Possibility)

Registries Research

Reality (Issue)

Clinical Research

Guideline (Rule)
A powerful tool for Translational Research

Microsurgery
Why microsurgery is in need in Living Donor Liver Transplantation in Children

S2 Graft (93g) (Am J Transpl, 2010)
Prof Ti-Sheng Chang, Father of Microsurgery in China
Prof Sun Lee, Father of International Society for Experimental Microsurgery (ISEM)

Experimental Microsurgery covered world-wide area as a powerful tool for Translational Research

- Immunology
- Pharmacology
- Ischemia/Reperfusion
- Microsurgical Devises
- Transplantation
- Tissue/Organ Engineering
- Minimum Invasive Surgery

Animals → Human

Experimental Microsurgery
Almost all organs can be transplanted in rats

Professor Eiji Kobayashi

1982  Graduation from Jichi Med Sch  
2001  Professor, CMM and Dep Surgery  
2003  Director, CEM, Jichi Medical Univ  
2009  Chief Scientific Adviser, Otsuka  
2014  Professor, Keio University, Sch of Med  

The 10th President; International Society for Experimental Microsurgery (ISEM)

In his Labo, you can muster excellent technique.
A powerful tool for Translational Research

Engineered Rats
GFP Animals in JMU

(2000)

マウス
(2000)

ラット
(2006)

ウサギ
(2007)

(2008)

Heart
Kidney
Liver

(Visible rays)
(ultraviolet rays)
A Powerful Tool for Translational Research
- Engineered Rats established in JMU-

Green Rat

Blue Rat

Red Rat

Firefly Rat

Neuroscience

In vivo bioimaging

Development

Gene Therapy
Transgenic Technology in Rats

1. A few success rate
2. Random Integration by chance!!

Green Rats

Heart

Kidney

Liver

(Hakamata Y & Kobayashi E. 2006)
Benefits in bio-imaging system using ‘fluorescence’

Aequorea victoria

Lung; 25 min after LPS injection

Transplanted lung immediately after re-perfusion
(Enomoto A, et al. Microsurgery 2007)

Differentiation from the fetal tissue

Neurosphere

Cerebral infarction

Migration

Red: Nestin
Red: GFAP

Injection of BMCs

Liver Injury Induced by Drugs

You can see the transdiffereciated cells

(Sato Y, et al. BBRC 2005)
Double Reporter (Red to Green) Tg; Cre/LoxP recombination system

- CAG promoter driven DsRed2/GFP double-reporter Tg rats
- Cre recombinase expressing Tg rats

Identification of muscle fusion events in limb transplantation model

Limb graft from Cre Tg rats

DsRed2/GFP double-reporter Tg rats

Donor

Recipient

Cre Tg Lox Tg

Bule Rats

Enbrio 21.5 days


(Skeletal Muscle, Heart)

(Inoue, Ohsawa et al. BBRC 2005)
Transplantation of neo-kidney into the LacZ Tg rat host

(a) Stereoscopic microscopy  
(b) X-gal assay  
(c) Electron microscopy  
(d) RT-PCR using FACS-gal assay

Proceeding of International Collaboration will encourage us very much!
Firefly Rat
Stem Cell Research
Using Bioimaging Rat and Pig
Luciferase Transgenic Ratの発光

Case the transplanted hepatocytes

Hepatectomized

Normal

Days after hepatocytes transplantation

(Hakamata Y, et al Transplantation 2006)
Luminescence Technology in preservation and transplantation for rat islet

(K Negishi et al. Islets 3(3):111-117 2011)
Luminescence Imaging of Regenerating Free Bone Graft in Rats

The Fate of Nonvascularized Fat Grafts: Histological and Bioluminescent Study

(Vascularized Graft)

(Non-Vascularized Graft)

Bone Marrow-Derived Mesenchymal Stem Cells Ameliorate Hepatic Ischemia Reperfusion Injury in a Rat Model

In Vivo Bioimaging Analysis of Stromal Vascular Fraction-Assisted Fat Grafting: The Interaction and Mutualism and Cells and Grafted Fat

Nude mice
SVF
Fat
WT-Rat
Luc-Rat

(Zhou SB, et al. Transplantation 2014)
In vivo bioreactor

Organ bud transplantation

繰り返しMSCを移入することで「自己化率」を高めることができる

Mouse
Metanephros

マウス腎臓

(Rat MSC injection)

(Matsumoto K, et al. Stem cell. 2012)
In vitro fabrication

Hypothermic temperature effects on organ survival and restoration

Real-Time Detection System for Perfect Microsurgery

“Firefly” Transgenic LEW Rat

Skin

Heart

Liver

Extremities

Small Bowel

Kidney
Shall we do our best for the suffering patients