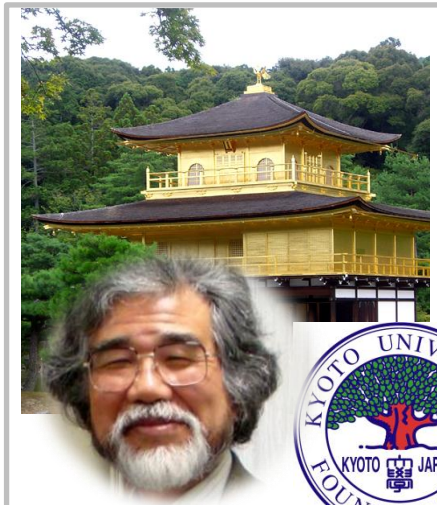
Company and Product Overview

Content

- ☐ Company
- ☐ iPS/ES cell culture reagents
- ☐ iPS cell derived functional cells

About Us

Kyoto



Tokyo

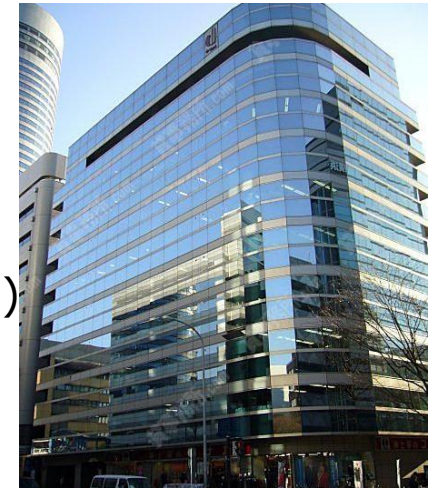
東京大学
THE UNIVERSITY OF TOKYO

Yokohama

ReproCELL

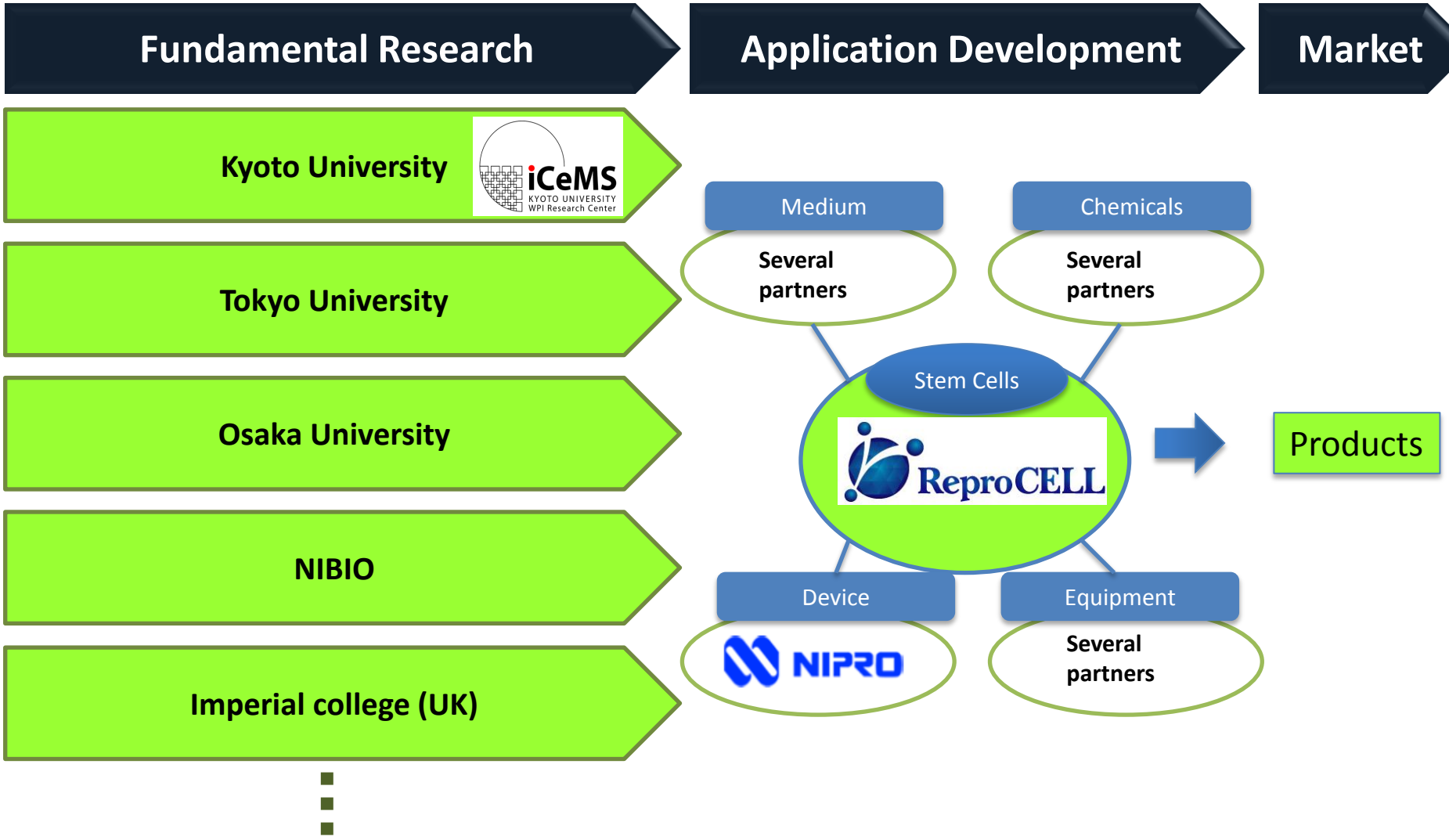
- Established in 2003
- In Yokohama
- 25 members (7 PhD)

Only Stem Cell Company in Japan



KANAGAWA

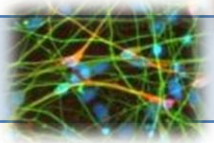
ReproCELL has strong scientific relationship with top institutes

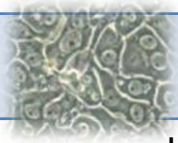
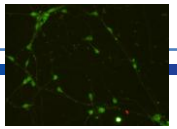


Lots of the world's 1st commercialized products

	Feb 2003	ReproCELL Inc. Established. Joint research agreement with Kyoto University and Tokyo University
1	Apr 2005	Research reagent business start: Primate ES cell medium
	Jul 2005	National granted project with Kyoto University and pharmaceutical companies "Drug screening and toxicity technology using human ES cells" (2005 to 2010)
2	Nov 2007	Human iPS cell invented by Prof. Yamanaka using Primte ES cell medium
3	Apr. 2009	Human iPSC-derived cardiomyocytes launch (The world's 1st)
4	Oct. 2010	Human iPSC-derived DA neuron launch (The world's 1st)
5	Apr. 2011	ReproFF2: Requires only 3-day culture work per week (The world's 1st)
	Apr. 2011	ReproCELL USA established in San Jose
	Apr. 2011	National granted project with Kyoto University and companies "Automated cell culture and quality control of stem cells" (2011 to 2015)
6	Spring 2012	Human iPSC-derived hepatocyte launch (The world's 1st)
7	Summer 2012	Human iPSC-derived cholinergic neuron and alzheimer's disease model neuron launch (The world's 1st)





Led by capable talents

CEO: Chikafumi Yokoyama, Ph.D

Sumitomo 3M, as a new project leader
McKinsey and Company Inc.
Ph.D. in chemistry from Tokyo University

Chairman of Stem Cell and Drug Discovery Institute

CTO: Yasuyuki Asai, Ph.D

Tanabe Pharmaceutical Co., Ltd.,
Ph.D. in Faculty of Biological Pharmacology
Postdoctoral fellow at Vanderbilt University Medical Center

Director: Yoshiyuki Yamakawa

HIBIKI Partners Co. Ltd., CEO
Sosei Co. Ltd., CFO
Nippon Life Insurance Company

Content

- ☐ Company
- ☐ iPS/ES cell culture reagents
- ☐ iPS cell derived functional cells

ReproCELL's reagents cover all steps of iPS/ES cell culturing

	Dish coating	Culturing			Passage	Cryo-preservation
Feeder-dependent	 ※ReproCoat	 ★MEF, SL10	 bFGF	 ※Primate ES cell medium	 ※Repro Stem	 ※Dissociation solution	 ※Freezing Medium
Feeder-Free	 ※Laminin-5	 bFGF	 ※ReproFF2			 ※Dissociation solution	 ※Freezing Medium

These products are the base of Kyoto University's iPS cell culture protocol

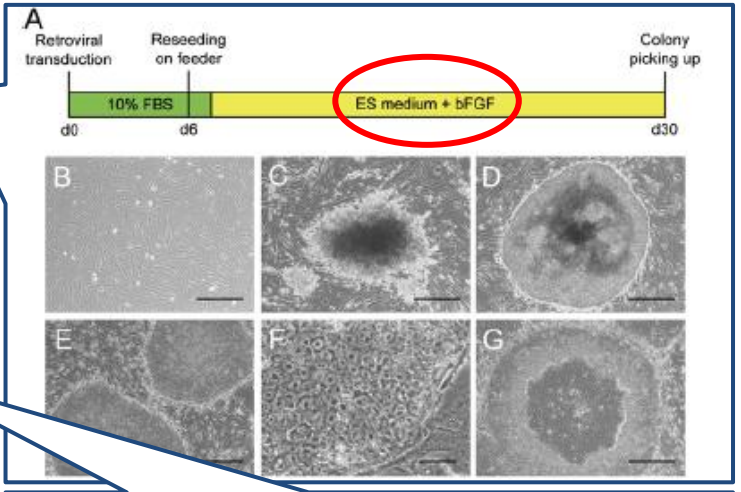
※ Offer 1 free sample per laboratory

★ Sorry, available only in Japan

1. Primate ES cell medium: Gold standard in Japan

Primate ES cell medium

- **Great scientific background**: Developed with Prof. Nakatsuji, iCeMS, Kyoto University and has 7 years track record
- **Gold standard in Japan**: Prof. Yamanaka used to establish the world's 1st iPS cell line and has been using heavily
- **Usable for various cell lines**: Highly compatible composition with popular medium NIH (United States) made public. E.g. KhES-1,2,3, H9, 201B7, 253G1 etc.
- **Ready to use**: just add bFGF to the bottle
- **Quality control**: conduct mycoplasma check and culture check(Un-differentiation, differentiation and growth speed)



hESC Medium

Vendor	Catalog Number	Volume
DMEM/F12	Invitrogen 11330-032	400ml
Knockout Serum Replacer	Invitrogen 10828-028	100ml
Non-essential amino acids	Invitrogen 11140-050	5ml
L-Glutamine	Invitrogen 25030-081	2.5ml
β-mercaptoethanol	Sigma 7522	.5µl

2. ReproStem: Cost conscious model of Primate ES cell medium

ReproStem

- **Further cost conscious model of Primate ES cell medium**: Developed to serve customer's lowering media cost needs
- **Highly compatible**: Composition is almost same as that of Primate ES cell medium. Therefore, highly compatible with Primate ES cell medium and NIH's medium
- **Some users prefer ReproStem to Primate ES cell medium**
  - Generally, days to be confluent are followings;
    - Primate ES cell medium: 3-4 days (2 Pa. / week)
    - ReproStem: 4-6 days (1-2 Pa. / week
  - But some cell lines grow at same speed with ReproStem as with Primate ES cell medium
  - Some cell line prefer ReproStem to Primate ES cell medium
- **Quality control**: conduct mycoplasma check and culture check(Un-differentiation, differentiation and growth speed)
- **Ready to use**: just add bFGF to the bottle at open

3. ReproFF2 (1/4): Feeder-Free&Weekend-Labor-Free Medium

ReproFF2

Conventional products		**ReproFF2**
Mon. Medium change		**Mon. Medium change**
Tue. Medium change	→	**Tue. –**
Wed. Medium change		**Wed. Medium change**
Thu. Medium change	→	**Thu. –**
Fri. Medium change		**Fri. Passage**
Sat. Medium change	→	**Sat. –**
Sun. Medium change	→	**Sun. –**

3.ReproFF2 (2/4): Feeder-Free&Weekend-Labor-Free Medium

ReproFF2

- **World's 1st concept: Media requires only 3-day work per week**
  - Halves the amount of medium use and cost
  - Reduce the weekend labor (This is critically important for companies)
- **Booming in Japan:** Only within 10 months after launch in April 2011, more than 130 laboratories have started to use ReproFF2 in Japan, US and Europe
- **Highly compatible**: Highly compatible with Primate ES cell medium, ReproStem and NIH's medium
  - Please note that within4-5th passage after feeder culture, cells might look not good. However, it is no problem and please continue and you will find the cells getting better
- **Can be used for sphere culture:** More scalable, easier and cheaper culture method
- **Quality control**: conduct mycoplasma check and culture check(Un-differentiation, differentiation and growth speed)
- **Ready to use**: just add bFGF to the bottle at open

3.ReproFF2 (3/4): Results of trial by cell line and other condition

For various cell lines and conditions, ReproFF2 can culture ES/iPS cells successfully

ES cells

Research institute	Cell line	Methodology for cell establishment	Result of culture	Coating matrix
Stem Cell Research Center, Institute for Frontier Medical Sciences, Kyoto University	KhES-1	N.A	○	Laminin-5
Research Institute National Center for Global Health and Medicine	KhES-3	N.A	○	Matrigel
Stem Cell Bank, Center for Stem Cell Biology and Regenerative Medicine, IMSUT	KhES-3	N.A	○	Matrigel
Department of Physiology School of Medicine, Keio University	H9	N.A	○	Matrigel

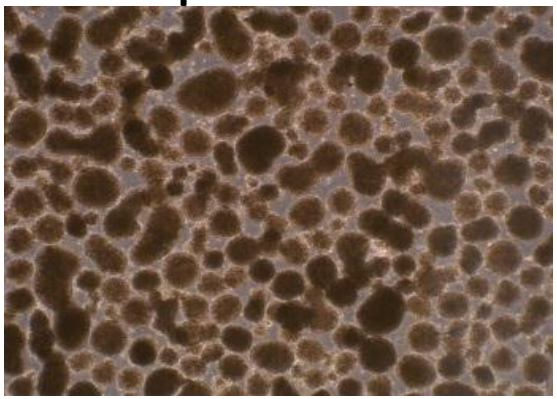
H7 and H14 are also OK

iPS cells

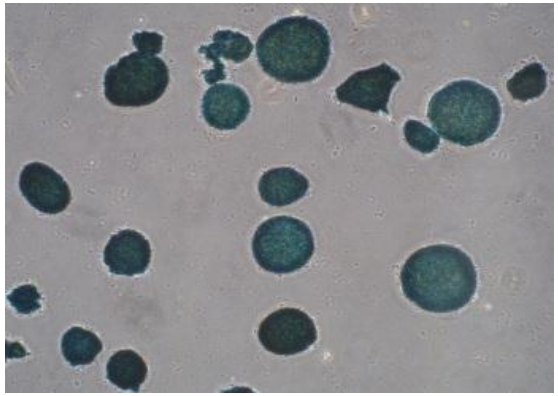
Research institute	Cell line	Methodology for cell establishment	Result of culture	Coating matrix
Institute of Molecular Embryology and Genetics	201B7	HDF/Retrovirus	○	Matrigel
Research Institute National Center for Global Health and Medicine	SeV-iPS	HUVEC/ Sendai virus	△: Other kind of cell also increased	Matrigel
RIKEN Center for Developmental Bilogy	Line1	N.A.	○	CellStart
	Line2	N.A.	○ : with Laminin-5 × :with CellStart. Cells were differentiated	Laminin CellStart
	Line3	N.A.	○ : with Laminin-5 × :with CellStart. Cells were differentiated	Laminin CellStart
Stem Cell Bank, Center for Stem Cell Biology and Regenerative Medicine, IMSUT	TkDA 3-4	HDF/4 Retrovirus	○	Matrigel
Department of Physiology School of Medicine, Keio University	201B7	HDF/4 Retrovirus	○	Matrigel

3.ReproFF2 (4/4): Can be also used for Sphere culture

Morphology of iPS cell in sphere culture



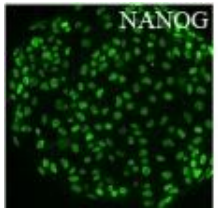
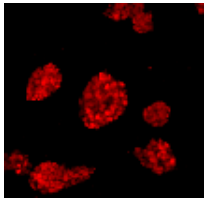
ALP staining : Positive



201B7
Pa.5

Merit	• **Easier technic**: No coating, No pipetting to dissociate colony softly • **Lower cost**: No coating solution, petri dish can be used • **Volume of dish and CO2 incubator will be more highly utilized** • Checking the increase of number of cells per same volume of media compared with attached culture
Abstract of protocol	• Start with attached culture in feeder-free media • Gather cells after dissociation • Make colonies' size into 70μ m by using cell strainer • When the size of spheres become approx. 250μ m, dissociate them by dissociation solution and cell strainer into 70μ m
Schedule	• **Under experiment on differentiation** • **Around the end of this January, 1st version of protocol will be made public on our website**

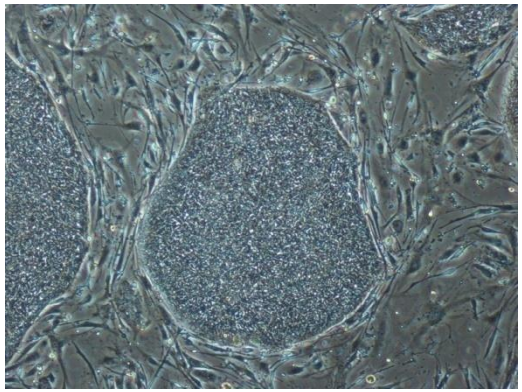
Other products*

Coating solution	FGF	Dissociation /Cryopreservation	Anti Nanog antibody
ReproCoat  • Standard in Kyoto university • 1kit for 4 media bottles	**bFGF**  • High quality • Ready to use • Very cheap • 1 kit for 10 media bottles	**Dissociation solution**  • Developed with and standard in Kyoto university • 1 kit for 0.5 medium bottle	**Anti human Nanog antibody**  • Globally popular
Laminin-5  • Human recombinant • No cell scraping • 4-5 kits for 1 medium bottle		**Freezing Medium**  • Developed with and standard in Kyoto university • 1 kit for 125 dish	**Anti mouse Nanog antibody**  • Globally popular

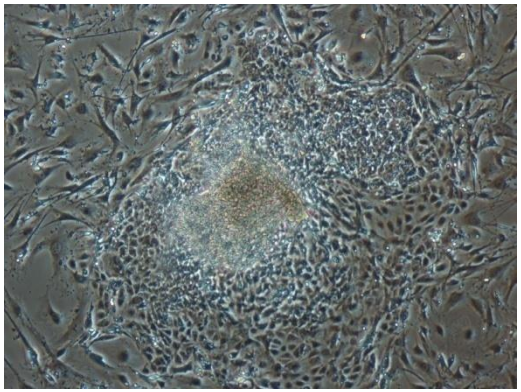
* For calculating required volume of each product, dish size is assumed as ϕ60

(Feeder)human iPS cell cultured by Primate ES cell medium

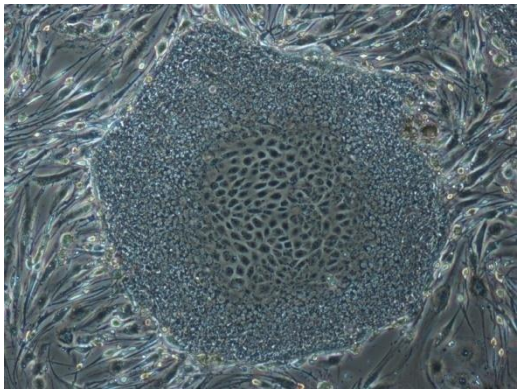
human iPS cell (201B7)/ MEF/ Primate ES Cell Medium+5ng/mL bFGF



Good colony



Outline of colony is unclear

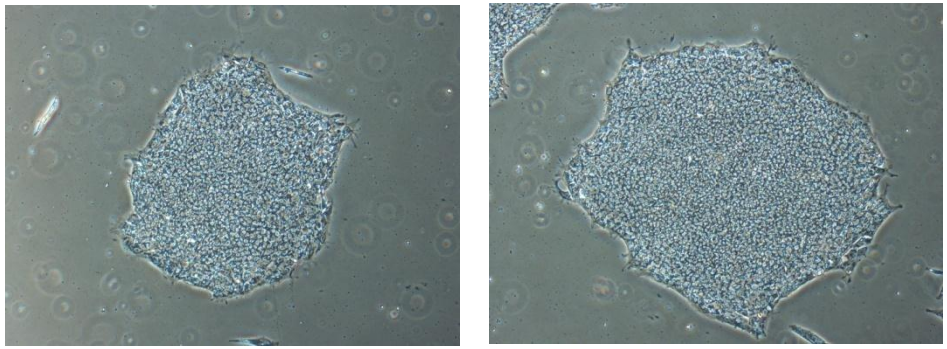


Some part with low density within colony

- At passage, if the ratio of bad colony is under 10%, it is no problem.
- If you mind it, mark the bad colonies and get rid of them or select only good colony at passage

(Feeder-free) human iPS cell cultured by ReproFF2

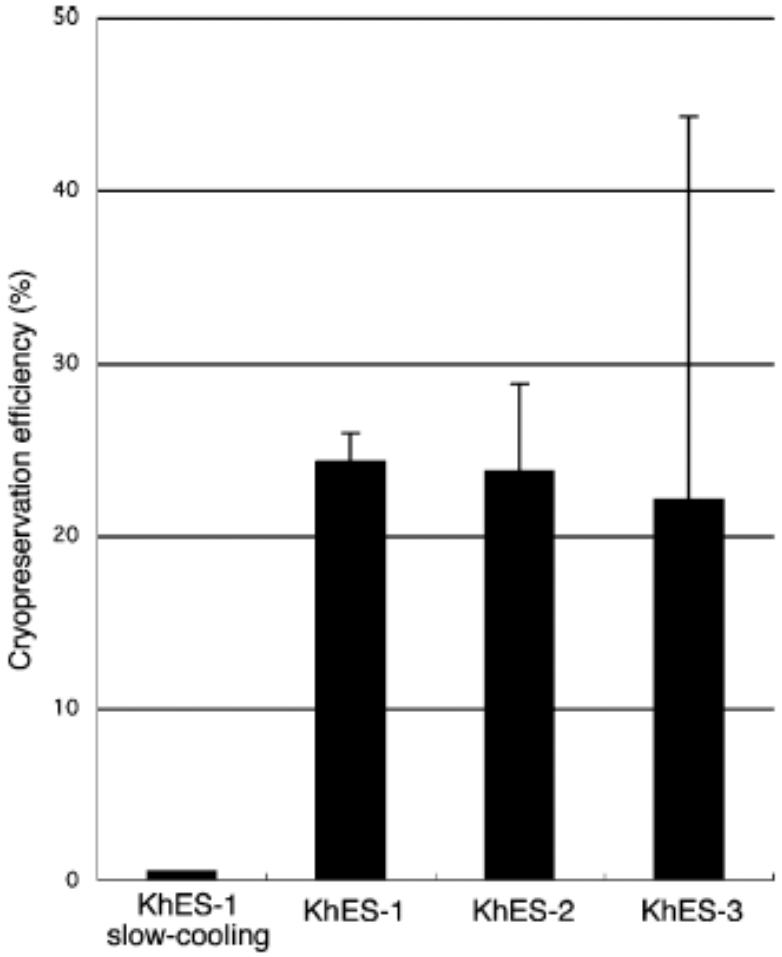
human iPS cell (201B7)/ / Laminin-5/ ReproFF2+5ng/mL bFGF



Good colony

- After passaging from feeder-dependent culture, within 4-5 passages, colony might not look good.
- However, please continue culturing after 6-7 passages, the colony will be good

Freezing medium – High viability



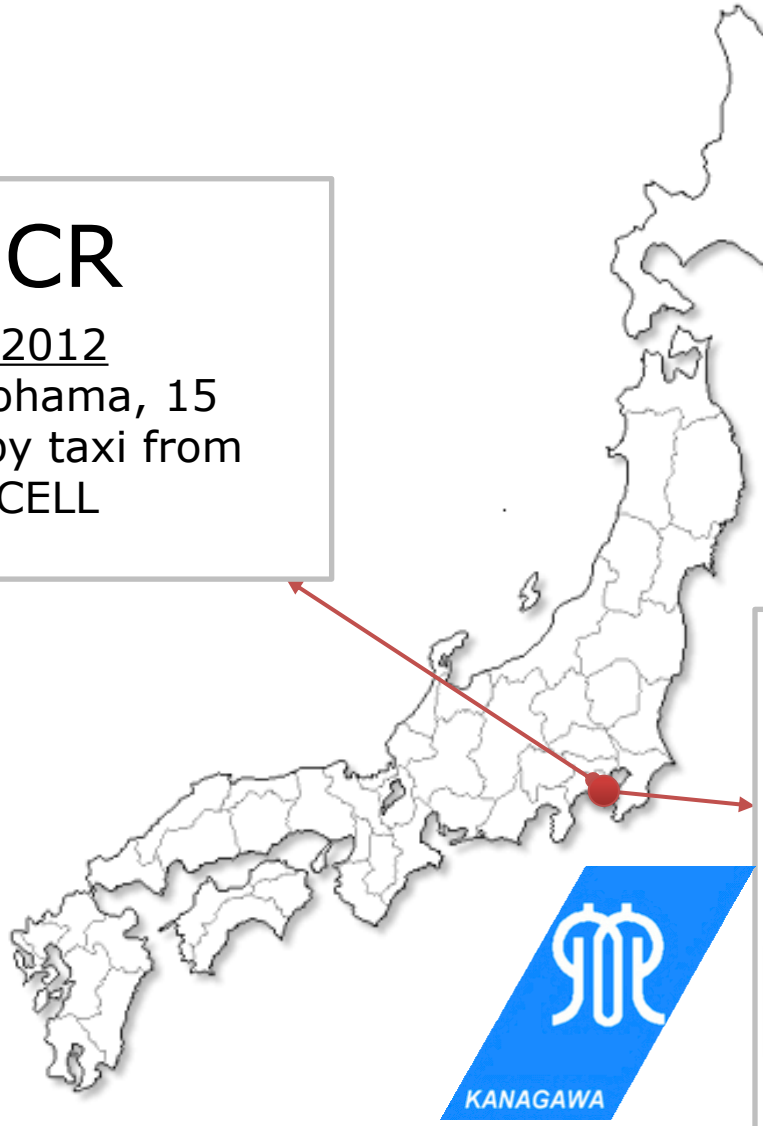
DMSO (Slow cooling)

Freezing Medium (Vitrification)

Please participate iPSC culture training during ISSCR

ISSCR

- June, 2012
- @Yokohama, 15 min. by taxi from ReproCELL



- We offer hands-on cell culture training during ISSCR everyday.
- Please book by the end of March
- 1 person for 1 labolatory

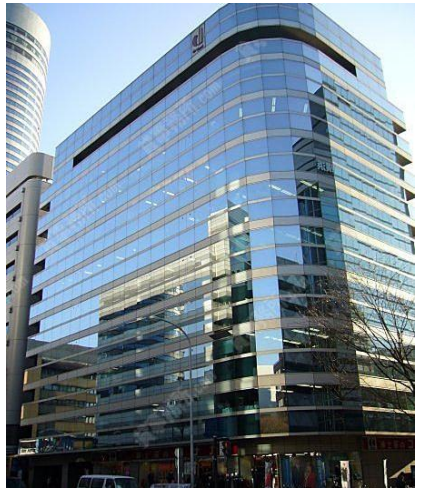
- Please also access our website with technical videos

http://www.reprocell.com/en/reagents/culture_movies/

ReproCELL

Yokohama

Only ES/iPS Cell Company in Japan



Product lists

#	Large classification	Middle classification	Product number	Product name
1	Stem Cell Research Regents	Cell Culture Regents	RCHEMD001	Primate ES cell medium (500mL)
2	Stem Cell Research Regents	Cell Culture Regents	RCHEMD001-S	Primate ES cell medium (100mL)
3	Stem Cell Research Regents	Cell Culture Regents	RCHEMD003-S	ReproFF (50mL)
4	Stem Cell Research Regents	Cell Culture Regents	RCHEMD004	ReproFF (500mL)
5	Stem Cell Research Regents	Cell Culture Regents	RCHEMD005	ReproStem (500mL)
6	Stem Cell Research Regents	Cell Culture Regents	RCHEMD005-S	ReproStem (100mL)
7	Stem Cell Research Regents	Cell Culture Regents	RCHEMD006	ReproFF2 (500mL)
8	Stem Cell Research Regents	Cell Culture Regents	RCHEMD006-S	ReproFF2 (100mL)
9	Stem Cell Research Regents	Cell Culture Regents	RCHETP002	Dissociation solution for human ES/iPS cells (30mL)
10	Stem Cell Research Regents	Cell Culture Regents	RCHETP001-S	Dissociation solution for human ES/iPS cells (3mLx2)
11	Stem Cell Research Regents	Cell Culture Regents	RCHEFM001	Freezing medium for human ES/iPS cells (25mL)
12	Stem Cell Research Regents	Cell Culture Regents	RCHEFM001-S	Freezing medium for human ES/iPS cells (1mL)
13	Stem Cell Research Regents	Cell Culture Regents	RCHEOT002	bFGF (25ug)
14	Stem Cell Research Regents	Cell Culture Regents	RCHEOT003	bFGF (250ug)
15	Stem Cell Research Regents	Cell Culture Regents	RCHEOT004	Laminin-5 (1ug) x6
16	Stem Cell Research Regents	Cell Culture Regents	RCHEOT004-S	Laminin-5 (1ug) x3
17	Stem Cell Research Regents	Antibody	RCAB001P	Anti mouse Nanog antibody (200uL)
18	Stem Cell Research Regents	Antibody	RCAB002P-F	Anti mouse Nanog antibody (100uL)
19	Stem Cell Research Regents	Antibody	RCAB003P	Anti human Nanog antibody (200uL)
20	Stem Cell Research Regents	Antibody	RCAB004P-F	Anti human Nanog antibody (100uL)
21	Stem Cell Research Regents	Cell Culture Regents	RCHECK002	Human/Primate ES/iPS cell culture kit

Content

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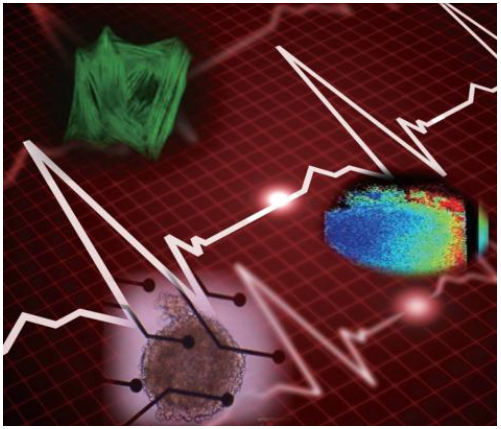
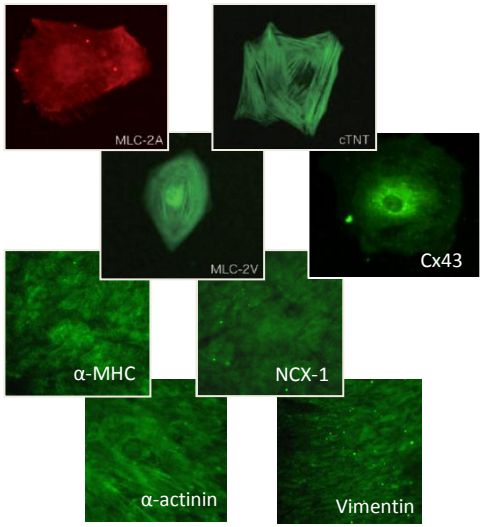
- ☐ iPS cell derived functional cells

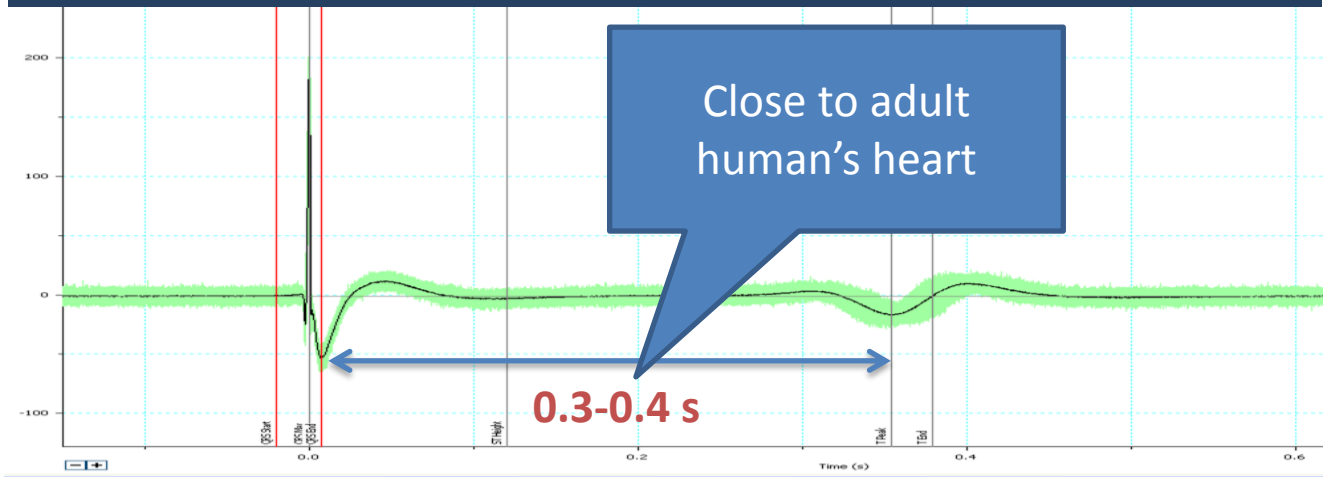
ReproCardio2: human iPSC derived cardiomyocyte



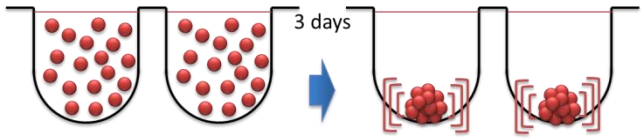
- The world's 1st commercial human iPSC-derived cardiomyocytes
- Developed by ReproCELL by using Kyoto university's technology
- Cells/Sheets/Clumps for a wide range of *in vitro* tests
- Reliable replication of *in vivo* characteristics



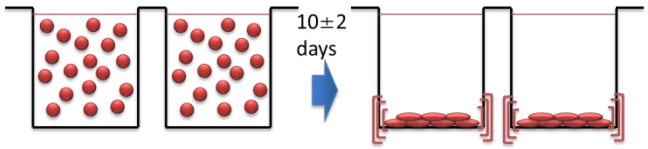
Electro Cardiogram



Form Clumps

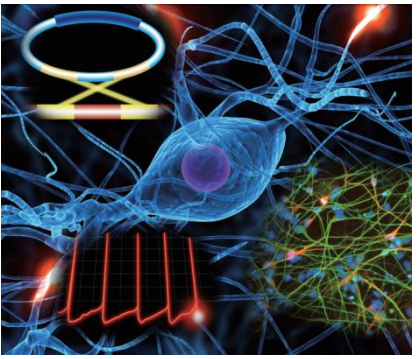


Form Thin Layers

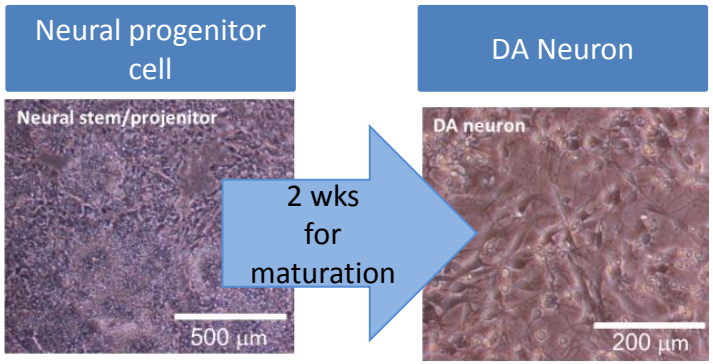


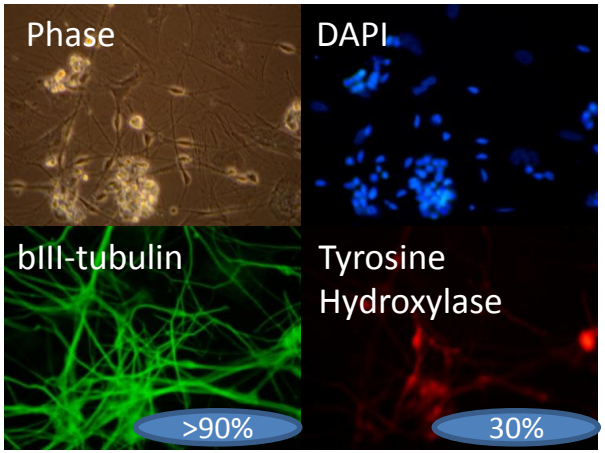
ReproCELL

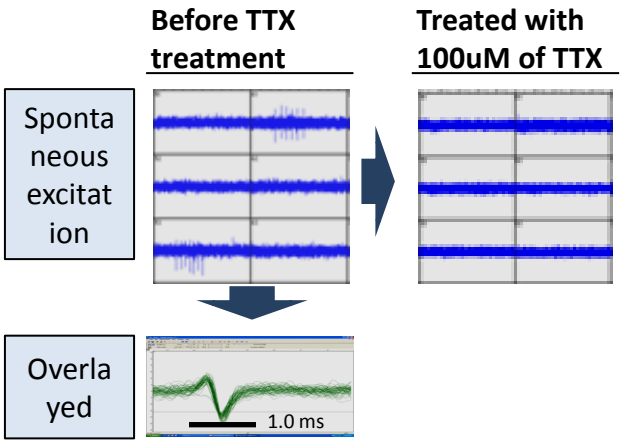
ReproNeuro DA kit: human iPSC derived DA neuron

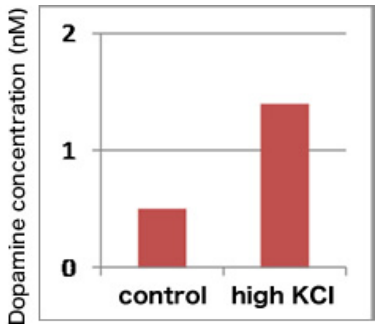


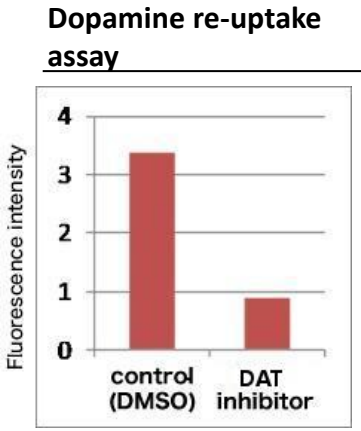
- The world's 1st commercial human iPSC-derived Neural cells
- Developed by ReproCELL by using Kyoto university's technology
- Disease model can be developed by DNA recombination
- Reliable source of functional human neurons



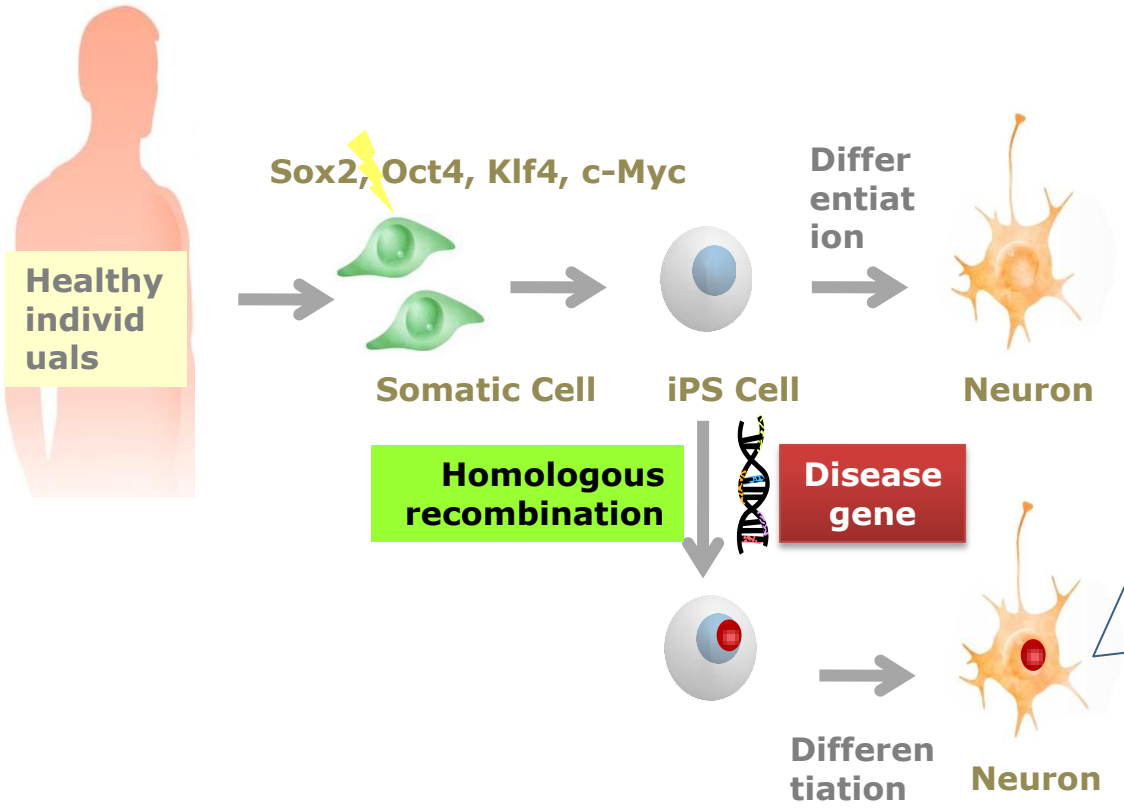




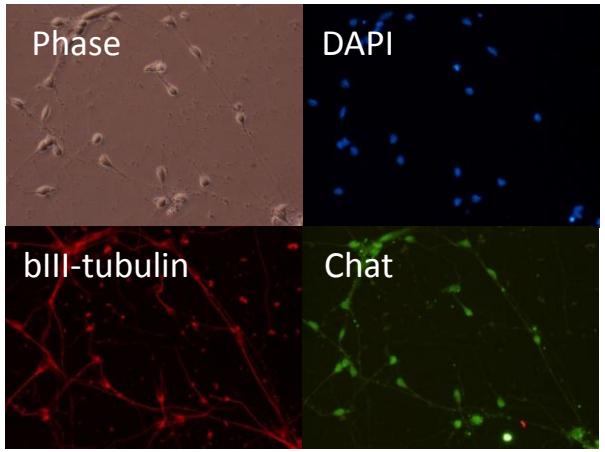




Cholinergic neuron and Alzheimer's disease model

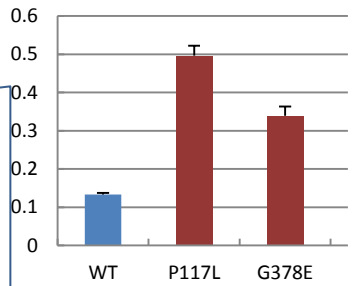


Cholinergic neuron

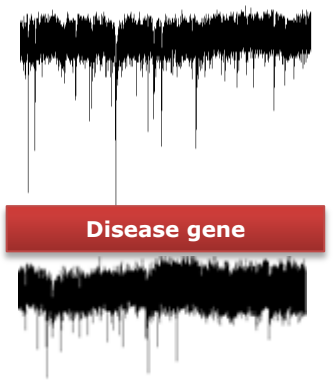


Alzheimer's disease model

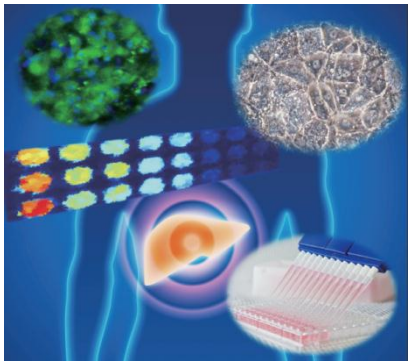
Ab42/Ab40 production



Spontaneous current

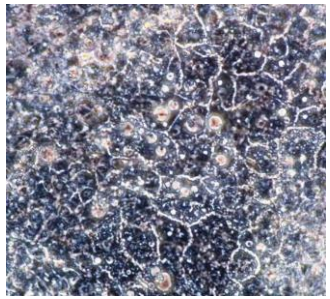


ReproHepato type A: human iPSC derived hepatocyte

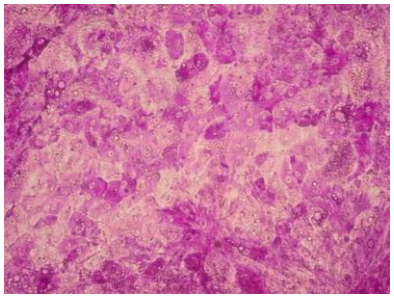


- High-purity human hepatocytes
- Robust CYP3A4, 2C19,2C9 activity comparable to that of the primary cells
- Convenient cryopreserved form
- Other Hepatocyte with 2D6 and 1A2 activity will also be launched

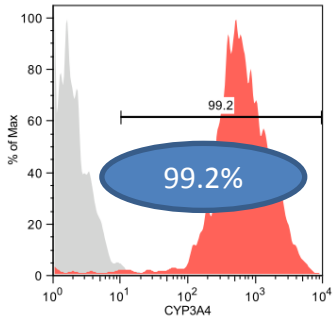
Hapatocyte, BF



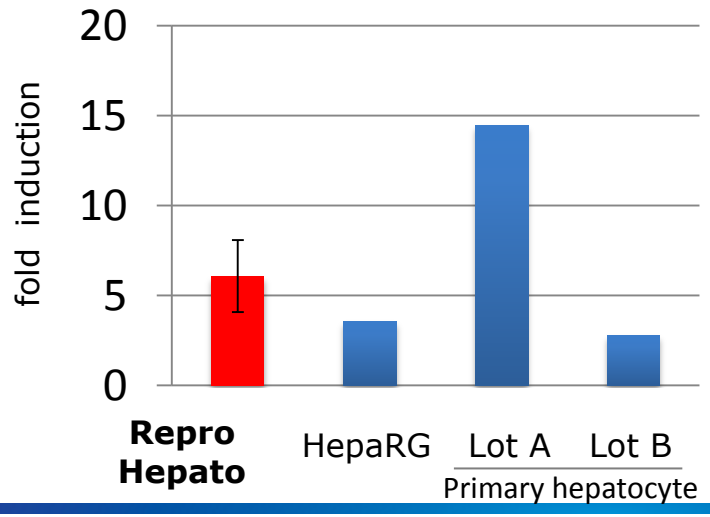
Hapatocyte, PAS



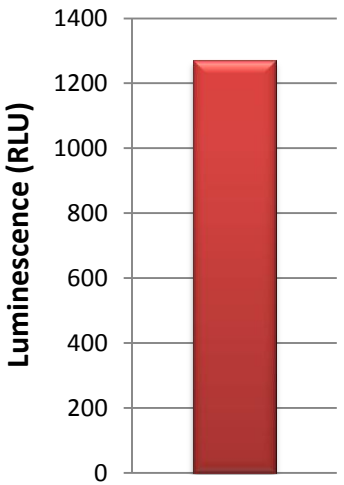
CYP3A4, FACS



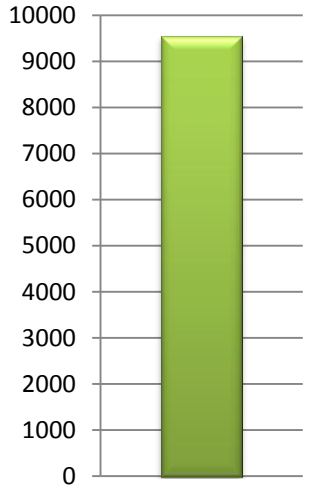
CYP3A4 induction at 5 uM Rifampicin



CYP2C9



CYP2C19



ReproCELL

Product lists

#	Large classification	Middle classification	Product number	Product name
22	Drug Discovery & Development	iPS derived cells	RCESD009	ReproCardio 2 small pack (1x10~5 cells for 10 wells in clump/layer form)
23	Drug Discovery & Development	iPS derived cells	RCESD011	ReproNeuro DA kit small pack (3x10~5 cells)
24	Drug Discovery & Development	iPS derived cells	RCESD007	ReproCardio assay medium (100mL)
25	Drug Discovery & Development	iPS derived cells	RCESD012	ReproCardio culture medium 2 (80mL)
26	Stem Cell Research Regents	Cell Culture Regents	RCHEOT001	ReproCoat (500mL)
27	Drug Discovery & Development	iPS derived cells	RCESD013	DA maturation kit (medium+additive A)
28	Drug Discovery & Development	iPS derived cells	RCESD014	DA maturation kit small (medium+additive A)
29	Drug Discovery & Development	iPS derived cells	RCESD015	DA thawing medium
30	Drug Discovery & Development	iPS derived cells	RCESD016	DA coat
31	Stem Cell Research Regents	Cell Culture Regents	RCHEOT001-S	ReproCoat (50mL)

Thank you very much

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- Technical support is available
- For effective support, please send photos of cells and detailed information on culture situation, as long as comfortable