REPROCELL

Improving human health through biomedical innovation and discovery

www.reprocell.com

Company Overview

REPROCELL was established in 2003 by preeminent Japanese university researchers, quickly becoming the leading stem cell research company in Japan. Soon thereafter, our products were employed by Professor Shinya Yamanaka (Nobel Laureate, 2012) for his pioneering development of induced pluripotent stem cells (iPSCs) at Kyoto University. We were the first company to offer iPSC-derived human cardiomyocytes, hepatocytes, and neuronal cells for research applications, and were listed on the JASDAQ (Japan) stock market in 2013.

To become a supplier and research partner for drug discovery, human tissue resources, and stem cell technologies, REPROCELL HQ (Yokohama, Japan) has since expanded through a series of commercial acquisitions. In 2016, the US holdings of Stemgent® Corporation (Lexington, MA) and Bioserve® Corporation (Beltsville, MD) were merged to form REPROCELL USA. As a leader in iPSC reprogramming technologies, Stemgent is recognized for developing the StemRNA™ Reprogramming Technology plus reagents to support the growth and differentiation of iPSCs. Bioserve is a company with an extensive biobank of over half a million human tissue samples to support biomarker identification, and drug research.

Also in 2016, REPROCELL Europe was established by merging the European holdings of Reinnervate® Corporation (County Durham, England) and Biopta® Corporation (Glasgow, Scotland). Reinnervate was known for the Alvetex™ brand of plasticware plates and membrane products, and for developing 3D models and applications for mammalian cell culture. Biopta is a contract research organization (CRO) that specializes in customized drug discovery assays using live human tissues secured in accordance with ethical guidelines .of governmental and medical agencies.

In 2018, the acquisition of Bioserve Biotechnologies India Corporation (Hyderabad) established Bioserve India, which offers DNA oligonucleotides and clinical diagnostic services in the areas of reproductive health and oncology. These services provide synergy with REPROCELL's stem cell technologies and innovative human tissue drug discovery services.

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Bioserve
Hyderabad, India
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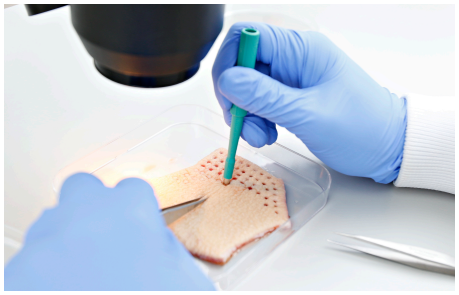
Cover photo: the REPROCELL *Centre for Predictive Drug Discovery*, Glasgow UK.

REPROCELL provides products and services across the entire drug discovery process

TARGET IDENTIFICATION	TARGET VALIDATION	LEAD IDENTIFICATION	LEAD OPTIMIZATION	PRECLINICAL SAFETY	CLINICAL TRIALS
Over 600,000 human samples	Functional target validation in diseased tissues	Stem cells and 3D models as human relevant systems	Demonstrate efficacy in human fresh tissues	Detect adverse effects in human tissue and compare directly to animal data	Troubleshoot clinical observations in living human tissue
			Predict human absorption or metabolism		Clinical grade stem cell services and products

De-risking the discovery process by increased use of human data

REPROCELL has products and services that cover the entire drug discovery workflow. Human biospecimens can be obtained from partner organizations, reprogrammed by our RNA technologies into iPSCs, and cultured using our media and reagents. These iPSCs can be differentiated into various somatic cell types and grown using special scaffolds or culture-plates to create 3D model systems that more closely mimic real human tissue. And finally, these bioengineered human tissue models or living human tissues can then be used for preclinical drug development, or troubleshooting clinical adverse effects.



Pictures from REPROCELL Europe's *Centre for Predictive Drug Discovery* in Glasgow, UK.
From top right, clockwise: One of our researchers making full-thickness human skin biopsies; Alvetex Scaffold used to bioengineneer 3D human tissues: one of our researchers removing cells from a freezer.

Our human tissue specimens and molecular services can accelerate **Target Identification**

TARGET IDENTIFICATION | TARGET VALIDATION | LEAD IDENTIFICATION | LEAD OPTIMIZATION | PRECLINICAL SAFETY | CLINICAL TRIALS

Human Tissue Specimens

REPROCELL has one of the world's largest commercial biorepositories of human tissue samples, including over 600,000 samples of frozen tissue, FFPE tissue blocks, whole blood, serum, plasma, RNA and DNA samples. The samples in our collection are linked to detailed clinical and demographic data from over 120,000 consented and anonymized patients spanning four continents.

In addition, our network of partner organizations provides broader access to additional rare samples and the ability to source material specific to your research needs through prospective collections.

Global BioRepository Inventory by Disease Type

Cancers	**Metabolic**	**Miscellaneous**
Brain	Diabetes	Asthma
Breast	Cardiovascular	Pneumonia
Cervical		Dementia
Colon	**Metabolic**	Renal Disease
Head & Neck	Lupus	Hepatic Injury
Leukaemia / Lymphoma	Rheumatoid Arthritis	Osteoporosis
Lung	Multiple Sclerosis	Sepsis
Ovarian	Psoriasis	**Other**
Prostate	Rhumatoid Arthritis	Controls
Renal		

We have it... **Our network has it...** **Or, we can collect it**

Each human tissue sample is provided with:

- Detailed demographic information
- Gold standard clinical diagnostic information
- Complete drug history, including adverse events
- Full pathology report, including H&E slides
- Complete phenotypic data

Patient recruitment and tissue collection:

- Governed by IRB protocols and HIPAA regulations
- Ethically collected and broadly consented
- Sample data anonymized from original consents

Molecular Services

REPROCELL has a suite of preclinical molecular services for the identification of genetic markers, validation of drug targets and correlation of clinical and molecular data to accelerate the development of new and safer drugs.

With CLIA-approved laboratories and over 20 years of custom service experience, you can trust our quality and data accuracy.

REPROCELL iPSCs are ideally suited for applications in **Target Validation** and **Lead Identification**

TARGET IDENTIFICATION | TARGET VALIDATION | LEAD IDENTIFICATION | LEAD OPTIMIZATION | PRECLINICAL SAFETY | CLINICAL TRIALS

Cell Reprogramming Products

Our latest research-grade reprogramming technology, the StemRNA™ 3rd Gen Reprogramming Kit provides you with clinically relevant RNA iPSC lines.

Footprint-free and highly efficient, the StemRNA™ Reprogramming Technology is the only RNA methodology optimized on three different cell types (fibroblasts, blood-derived and urine-derived progenitor cells) and enhanced by both microRNAs and interferon-response suppression mRNAs.

The pluripotency potential, stability, and growth of iPSCs generated by the research-grade 3rd Gen StemRNA reprogramming technology is unrivalled and even uses an entirely xeno-free protocol for fibroblast reprogramming.

Top Products

StemRNA-3rd Gen Reprogramming Kit	00-0076
NutriStem® hPSC XF Medium*	01-0005
iMatrix-511 Stem Cell Culture Substrate*	NP892-11
NutriFreez D10 Cryopreservation Medium (50 mL)*	01-0020-50

*recommended for use with kit 00-0076

The StemRNA-3rd Gen Reprogramming Kit

Services for Reprogramming and Custom Primary Cell Derivation

REPROCELL can also source healthy or diseased skin, blood, or urine samples and derive target cell lines to generate iPSC lines. Multiple iPSC clones are genetically analyzed, validated for pluripotency, and profiled for donor authenticity.

In addition, our stem cell scientists can customize your service project based on your needs.

Our custom iPSC services use StemRNA™ Reprogramming Technologies which are available to both academic and industrial customers. For all research activities, use of the iPSCs are royalty-free.

Besides reprogramming, REPROCELL also offers services for expanding and differentiating your iPSC lines into various somatic cell types.

Our GMP iPSC Master Cell Bank manufacturing service can accelerate your journey from **Target Identification** to **Clinical Trials**

TARGET IDENTIFICATION | TARGET VALIDATION | LEAD IDENTIFICATION | LEAD OPTIMIZATION | PRECLINICAL SAFETY | CLINICAL TRIALS

GMP-grade Stem Cells

Our stem cell experts can manufacture GMP iPSC MCBs which are compliant with the regulatory standards and guidelines of FDA, EMA, and PMDA.

With global access to human tissue samples, we can procure the tissues needed for your cell therapeutic, perform the necessary viral and donor profile screenings, and derive the primary fibroblast culture. Using our propriety footprint-free RNA reprogramming technology, our stem cell experts can generate a clinically compliant iPSC seed stock using GMP-grade media and reagents. Clonal seed iPSC lines are available for evaluation by the client before committing to the MCB manufacturing step.

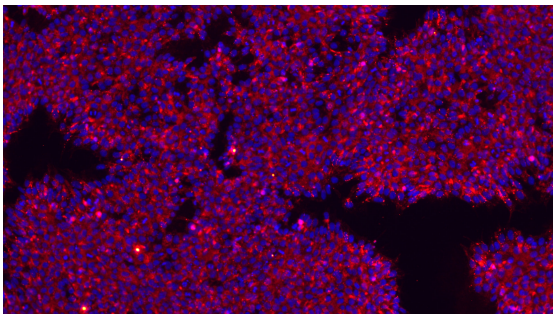
Under strict quality control measures, these seed iPSCs are expanded in a GMP environment to manufacture a Master Cell Bank. The final GMP iPSC lines are exclusive to the Sponsor; available only for your therapeutic project.

Alternatively, you can choose from our off-the-shelf seed stock iPSC lines.

Compliant with FDA, EMA, and PMDA

At REPROCELL, our GMP iPSC Master Cell Banks are manufactured in accordance with standards and guidelines of the three key regulatory agencies FDA, EMA, and PMDA.

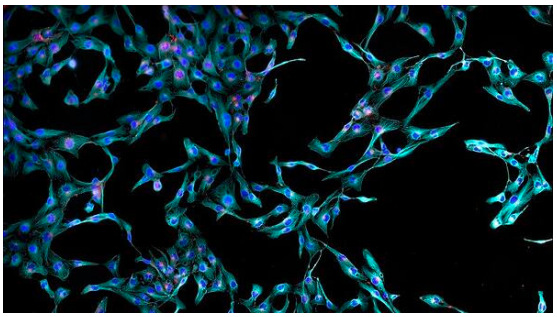
Our iPSC experts will provide the necessary quality and regulatory documents such as batch records, quality technical agreement, study reports, and COAs for your GMP iPSC MCB.



Commercial licence available

All our tissue donors have fully consented to clinical and commercial use.

REPROCELL provides the necessary clinical and commercial license for your project – making us a hassle-free one-stop solution provider for your clinical iPSC needs.



Our CRISPR-SNIPER gene editing service has a 97% success rate – even with challenging edits

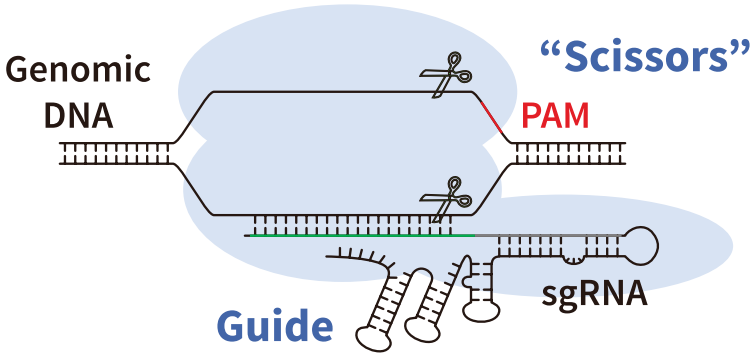
TARGET IDENTIFICATION | TARGET VALIDATION | LEAD IDENTIFICATION | LEAD OPTIMIZATION | PRECLINICAL SAFETY | CLINICAL TRIALS

CRISPR-SNIPER Gene Editing Service

In collaboration with GenAhead Bio, REPROCELL offers complementary state-of-the-art gene editing with our CRISPR-SNIPER Gene Editing Service.

CRISPR-SNIPER offers streamlined screening for positive results, resulting in high efficiency, high success rate editing. This service is ideal for challenging projects, such as creating single base changes, editing only one of a closely related set of genes, or isolating both homo- and hetero-allelic clones.

When combined with our custom tissue procurement and stem cell reprogramming in addition to differentiation services, genome editing provides concept-to-assay support for iPSC gene modification.



Comparison of Screening Methods

Condition	Positive Clones
SNIPER Screening	**20-30+%**
Traditional Screening	0.1-1%

REPROCELL's differentiated cell products, reagents and services are particularly useful to support research efforts in **Lead Optimization** and **Preclinical Safety**

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Stem Cell Culture Products

From our Dissociation Solution to ReproFF2 medium for feeder-free culture, REPROCELL original media are reliable and of high quality. For cultivation, dissociation, and freezing, we have a cell culture media right for you.

3D Cell Culture Products and Services

Technologies for cultivation of cells in 3D are becoming increasingly important in disease modelling, artificial organs, and drug discovery applications.

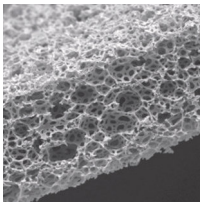
REPROCELL offers multiple 3D products and formats from which to choose. Alvetex™, REPROCELL's award-winning synthetic cell-culture scaffolds, are available in individual inserts, multiwell plates, or other configurations. EZSPERE® non-adherent microwell plates (Asahi Glass Company) promote formation of hundreds or thousands of aggregated cell spheroids.

For optimized iPSC suspension culture, the 3D Magnetic Stir and Disposable Bioreactor System (ABLE Corporation) is an outstanding option for growing 5 mL to 500 mL of batch cultures.

AteloCell® (Koken Pharma Corporation) is a cell culture scaffold made entirely from natural bovine collagen in the shape of discs and sponges.

Top Culture Media Products

Dissociation Solution	RCHETP002
NutriStem® hPSC XF Medium*	01-0005
StemFit AKO2N (Japan only)	NP892-11
StemFit Basic O3 Medium	ASB03
StemFit Basic O4 Complete Type	ASB04CT
StemFit for MSC	AS-MSC
Primate ES Culture Medium	RCHEMD001



Alvetex Scaffold membrane structure

Alvetex Scaffold 24 well insert

ABLE 500 mL Bioreactor

AteloCell sponges and scaffold structure

Cell culture applications are important in nearly all stages of drug development from **Target Validation** through **Preclinical Safety** assessment

TARGET IDENTIFICATION | TARGET VALIDATION | LEAD IDENTIFICATION | LEAD OPTIMIZATION | PRECLINICAL SAFETY | CLINICAL TRIALS

Cell Differentiation Products and Services

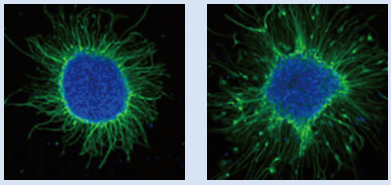
As a pioneering company in the production of iPSC-derived cells, REPROCELL has developed normal and disease-model cells (from patients with relevant diseases) of various types including neurons, hepatocytes, and cardiomyocytes. Our expertise and robust manufacturing processes ensure reproducible products and mature cell types that are electrophysiologically responsive.

REPROCELL's current stem cell product and service offerings are built around our proprietary Stemgent StemRNA™ 3rd Gen technology. This technology has been used to generate our StemRNA™ Neuro product line, of which Alzheimer disease model cells are also available. We also have a range of media and small molecules for stem cell research.

StemRNA™ Neuro – iPSC-derived Differentiated Neurons

REPROCELL's Stemgent StemRNA™ Neuro are differentiated iPSCs using proprietary technologies that result in a mixed population of neuronal cell types.

- World's first commercially available iPSC-derived human neurons
- Displays highly complex networked morphology with synaptic junctions
- Alzheimer disease options are available
- Clonally derived, highly consistent lot-to-lot performance, and stable phenotype



Outgrowth of Neurites from StemRNA Neuro cells (left) and StemRNA Neuro AD-Patient cells (right)

Reagents for Stem Cell Research

REPROCELL provides a single source of critical reagents for stem cell biology research. Each of our trusted brands is known for quality and consistency.

Our catalog of small molecules includes:

- GSK-3β inhibitors like CHIR99021
- Rho-kinase (ROCK) inhibitors like Y27632
- BMP inhibitors like LDN-193189

As well as many other Stemolecules™ for stem cell research. Our portfolio of Stemfactor™ cytokines and growth factors include basic FGF, LIF and Activin A.

Top Small Molecules

Stemolecule CHIR99021	04-0004
Stemolecule Y27632	04-0012
Stemolecule SB431542	04-0010
Stemolecule PD0325901	04-0006
Stemfactor FGF basic	03-0002
Stemfactor Human LIF	03-0016-100
Stemfactor Human Activin A	03-0001

REPROCELL provides products and services across the entire drug discovery process

TARGET IDENTIFICATION	TARGET VALIDATION	LEAD IDENTIFICATION	LEAD OPTIMIZATION	PRECLINICAL SAFETY	CLINICAL TRIALS
Over 600,000 human biospecimens from 120,000 donors	Functional target validation in disease tissues	Stem cells and 3D models as human relevant systems	Fresh tissue assays used to predict efficacy, absorption or metabolism	Detect adverse effects in human tissue and compare to animal data	Troubleshoot clinical observations in living human tissue

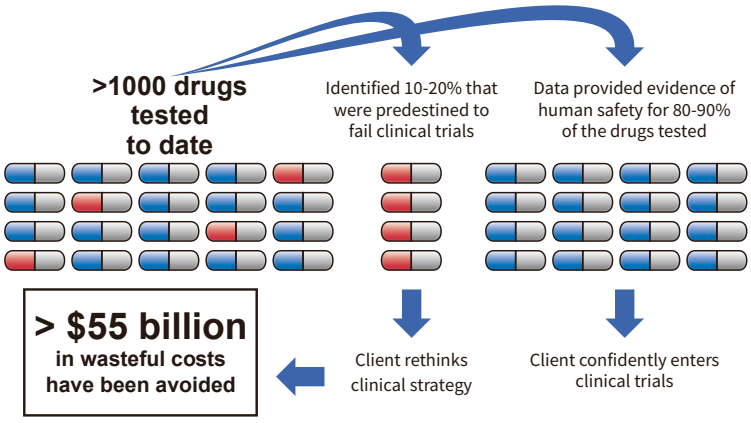
Drug Discovery Research Services

REPROCELL (previously Biopta) has been providing contract research services to the pharmaceutical industry since 2002 and has established itself as the world leader in the use of fresh functional human tissue research.

Our pharmacologists have a broad expertise in all areas of human tissue research, including sourcing, handling, and end point analysis. By predicting the safety, efficacy, absorption, or metabolism of compounds in phenotypically-relevant healthy and diseased human tissues, we generate data that can de-risk your drug development programs.

As owner of the industry's largest catalog of human functional tissue assays, we can customize experimental protocols to meet your specific needs. Having this insightful preclinical data early in discovery and development will help you to reduce the number of compounds that fail in the later stages; we estimate that since our establishment, we have helped Pharma save over $55 billion research dollars.

REPROCELL's human tissue technology predicts clinical success by using the closest possible model of drug behavior in humans



Lab Testing Capabilities include:

- IBD
- Skin Disease
- ADME DMPK Assays
- Gastrointestinal Motility
- Species Comparisons
- Cardiovascular
- Respiratory
- Genitourinary
- Neuronal

REPROCELL

Improving human health through biomedical innovation and discovery

bioserve

- Extensive biorepository of human tissue samples
- Network of clinical sites for prospective sample collection
- Molecular services

stemgent

- RNA reprogramming systems and services
- Reagents for pluripotent cell culture and differentiation
- Extensive portfolio of small molecules

alvetex

- 3D cell culture technology creating *in vivo*-like cell environment
- Protocols for stem cell, oncology and other tissue research applications

biopta

- Experts in human tissue research services for drug development
- Predictive safety, efficacy and ADME assays in human and animal tissues

Improving human health through
biomedical innovation and discovery

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