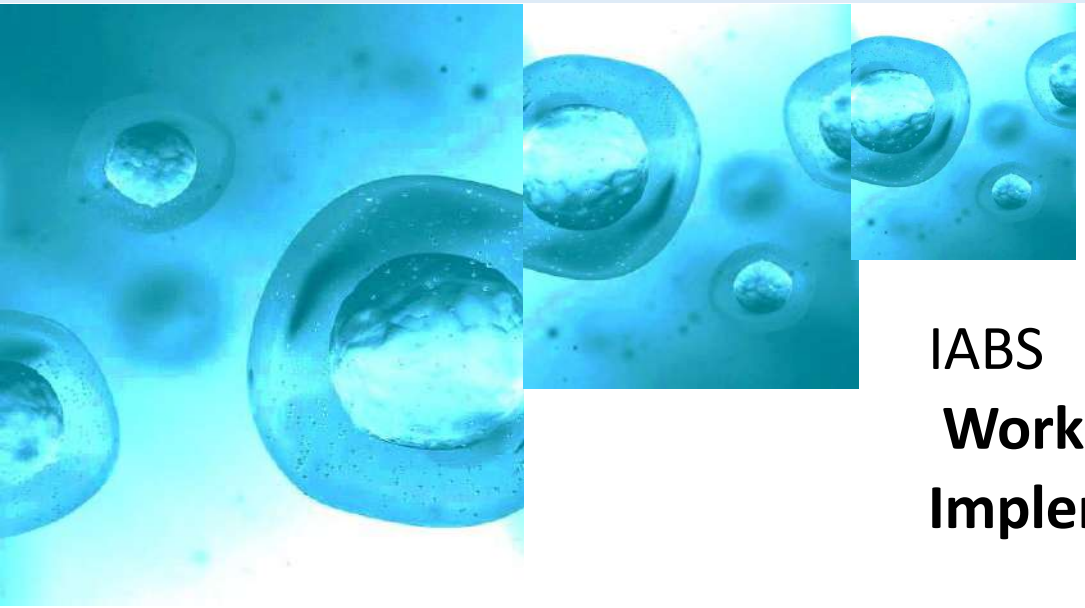
Quality by Design (QbD)-based Cell and Gene Therapy (CGT) product manufacturing and life cycle management



IABS

Workshop on Global Harmonization of Specification: Implementing A Patient-Centric, Enhanced Control Strategy

Cyto-Facto Inc. CEO
Kobe Univ. Dept of Science Technology and Innovation Project Professor

Shin Kawamata

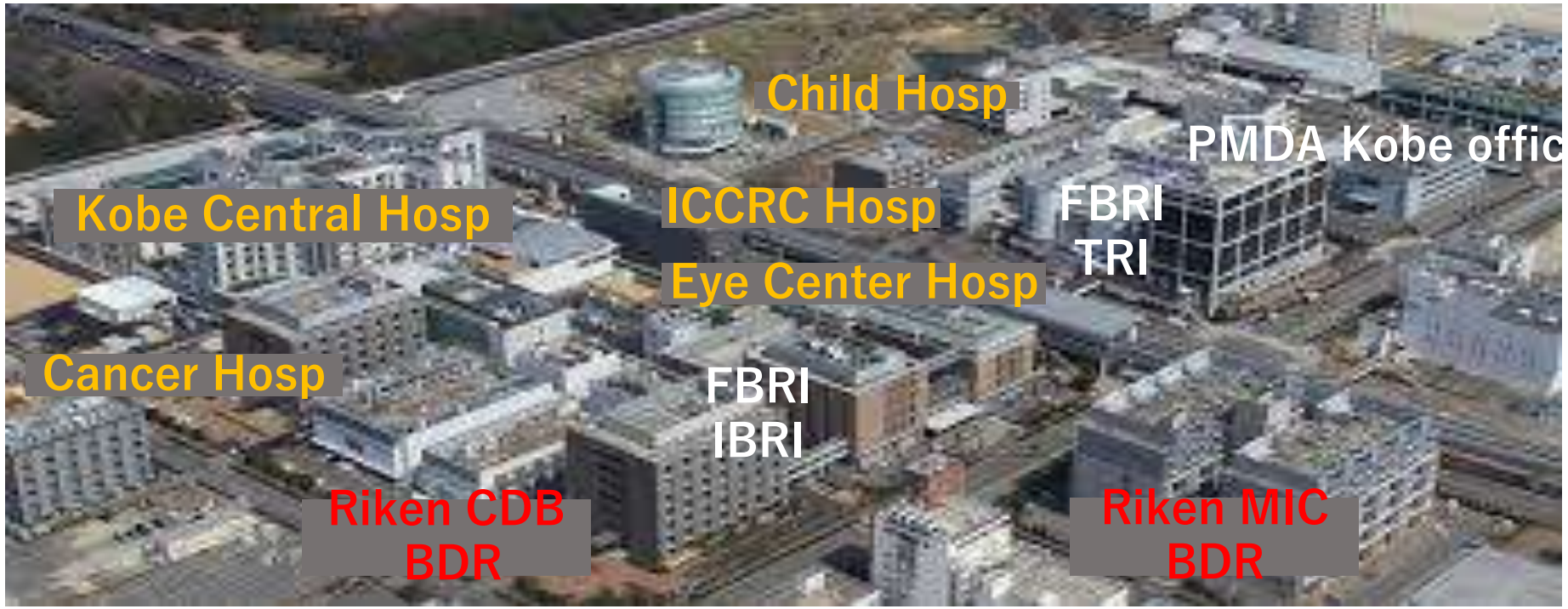
2025 0624

Introduction of CMO/CDMO company Cyto-Facto Inc.

Cyto-Facto Inc.

Cyto-Facto Inc. is a spinoff company

from Foundation for Biomedical Research and Innovation (FBRI)
that aims to support Kobe BioMedical Innovation Cluster project



Kobe BioMedical Innovation Cluster in 2023

2 Riken basic research centers

→ Translational Institution FBRI

5 universities and collages

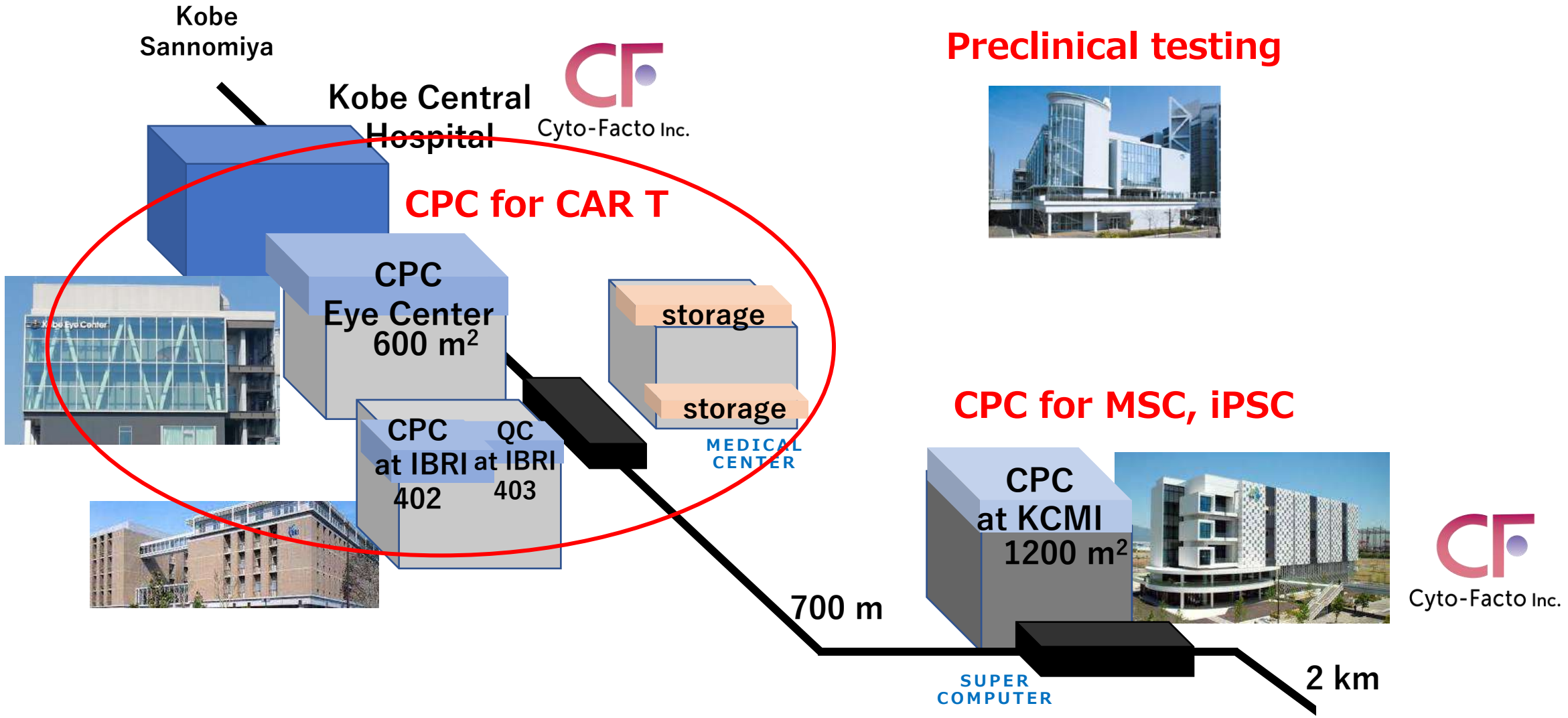
5 Hospitals with 1600 beds

PMDA branch office

360 Biomedical companies

Cyto-Facto

Cell manufacturing facilities of Cyto-Facto Inc.



CMO/CDMO business experience of Cyto-Facto (Its predecessor, the RDC of the FBRI)

2014	Launched CAR-T CMO project as R&D Center for Cell Therapy (RDC) of the FBRI. Technology transfer of CAR-T production (Kymriah®) by Novartis.
2017	Cell Processing Center in compliance with PIC/S GMP in the EC building in service.
2018	Began production of the clinical product Kymriah® for the Japanese market.
2020	Obtained approval for manufacture and sale of regenerative medicine products from HA. Commercial production of Kymriah® started.
2021	Technology transfer of MSC production (FF-31501) by Fujifilm.
2022	Completion and operation of the Cell Processing Center (CPC) on the 5th floor of KCMI
2023	FF-31501 investigational product manufacturing began. Several process development projects for CAR-T, MSC manufacturing started.

CPC in the Eye Center (EC) building. 6F

CPC in the Kobe Center for Medical Innovation (KCMI) building. 5F

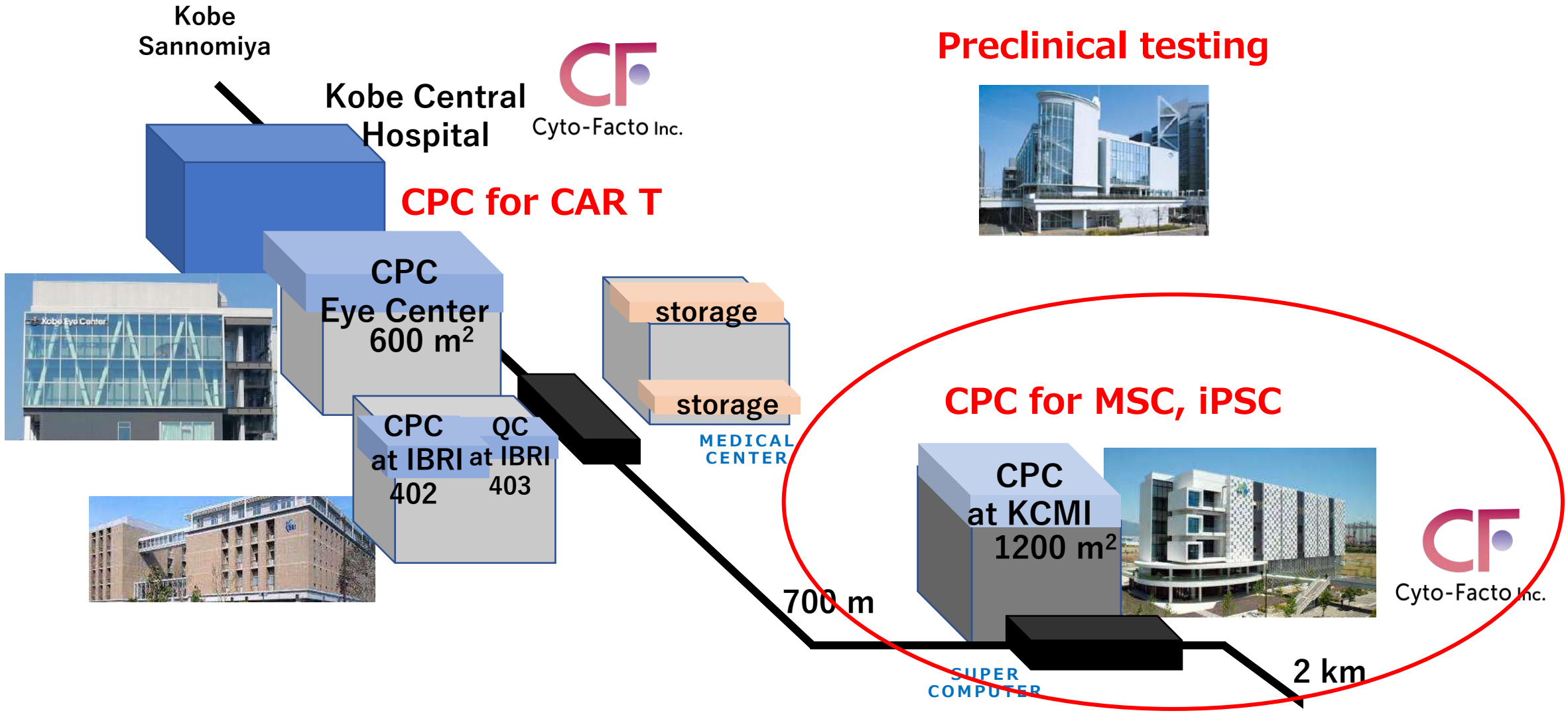
Cyto-Facto (its predecessor, the RDC of the FBRI) is the first Asian company to manufacture commercial CAR-T products in compliance with PIC/S GMP. Cyto-Facto has accumulated experience in manufacturing technology know-how and has launched several cell & gene manufacturing pipelines, including CAR-T, iPSC-based cells and mesenchymal stem cells (MSCs) of various developmental stages.

Introduction of Cell Processing Center

PIC/S GMP compliance manufacturing facility
That allows international shipment
Shipping record to Australia

Introduction of Cell Processing Center

Cell manufacturing facilities of Cyto-Facto Inc.



CPC facility in KCMI 5F

FUJIFILM Value from Innovation　Healios

SINFONIA

5CPCs
Central QC Room
Material Storage Room

Total 1,200㎡

・Clinical Trial of Autologous MSC

・Clinical Trial of eNK derived from iPSC

・Central QC Room

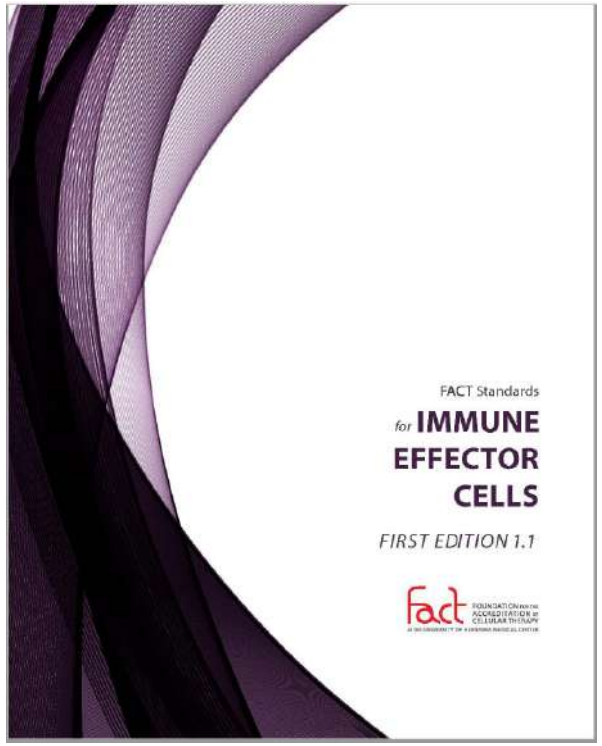
How can we overcome heterogeneity in quality of Patient sample?

The CAR-T therapy in Japan was started in 2018 through the network of JSTMCT

Introduce FACT - Standards for IMMUNE EFFECTOR CELLS to Japanese apheresis sites

Set up and open apheresis sites in Japan for Kymriah manufacturing through the network of Japan Society of Transfusion Medicine and Cell Therapy under the technical support from NPKK.

All of the apheresis sites opened in Japan were set up based on the recommended plans stated in the Q&A in the journal of JSTMCT and web HP.



JSTMCT
The Japan Society of Transfusion Medicine and Cell Therapy

Keio Univ. Hemato
Dr. Tanozaki

Kyoto Univ.Hemato
Dr. Arai

Kyoto Univ. Hemato
FBRI
Kawamata

Network of ARO was utilized to organize the apheresis/hospital sites for CAR-T therapy in Japan

FBRI chairs the Academic Research Organization Liaison Council for Cell Processing Center.

The 17 major academic/governmental medical centers for cell therapy participate Liaison Council.

FBRI promotes the supply of Kymriah and collect the therapy-related issues need to be fixed through this network.

Chaired by FBRI Kawamata

Cyto-Facto has a prestigious Kymriah manufacturing record, with manufacturing success rate of 95% (123 batches/129 batches)

ORIGINAL PAPER

Risk factors for CAR-T cell manufacturing failure among DLBCL patients: A nationwide survey in Japan

Tomoyasu Jo[1,2] | Satoshi Yoshihara[3,4] | Yoshiki Okuyama[5] | Keiko Fujii[6] | Tomoko Henzan[7] | Kaoru Kahata[8] | Rie Yamazaki[9] | Wataru Takeda[10] | Yoshihiro Umezawa[11] | Kentaro Fukushima[12] | Takashi Ashida[13] | Minami Yamada-Fujiwara[14] | Ryo Hanajiri[15] | Noboru Yonetani[16] | Yuma Tada[17] | Yuji Shimura[18] | Hidekazu Nishikii[19] | Norio Shiba[20] | Naoya Mimura[21] | Jun Ando[22] | Takayuki Sato[23] | Yasuhiro Nakashima[24] | Junko Ikemoto[4] | Keita Iwaki[14] | Shin-ichiro Fujiwara[25] | Masaki Ri[26] | Tokiko Nagamura-Inoue[27] | Ryuji Tanosaki[8] | Yasuyuki Arai[1,2]

BJHaem BRITISH JOURNAL OF HAEMATOLOGY

British Journal of Hematology
2023 April 13 Jo et al

Table 1 revised

Factory	2019-2021 Dec	Successful	Failed	successful rate
Novartis Morris Plains NJ US		255	24	91%
Cyto-Facto (FBRI) Kobe Japan		123	6	95%

CAR-T manufactured and infused to patents

Total 519 cases

manufacturing

DLBCL 438 cases

B-ALL 81 cases

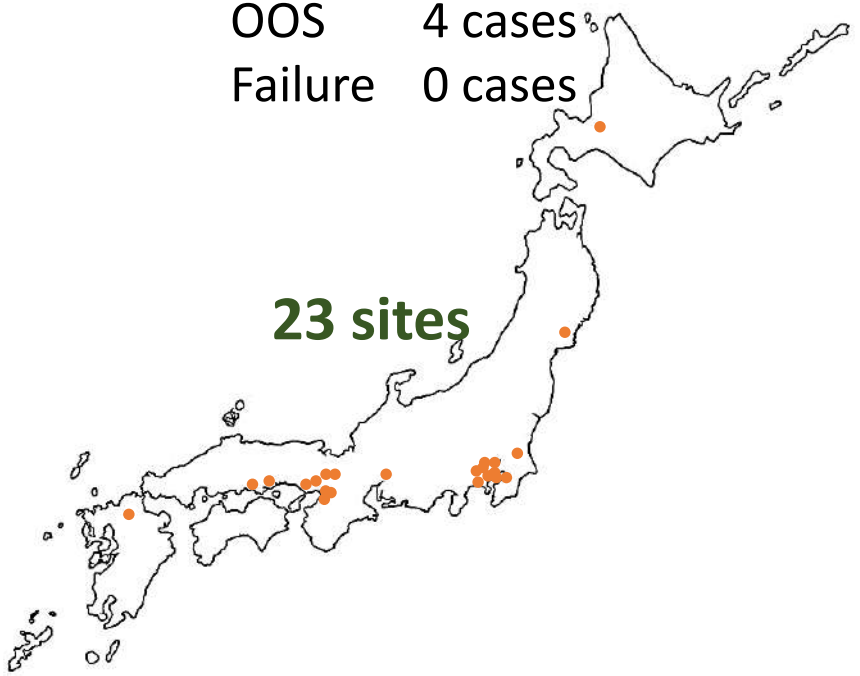
Excluding 30 OOS cases

Excl. OOS DLBCL 408 cases

Success 378 cases ⟺ Failure 30 cases

compare

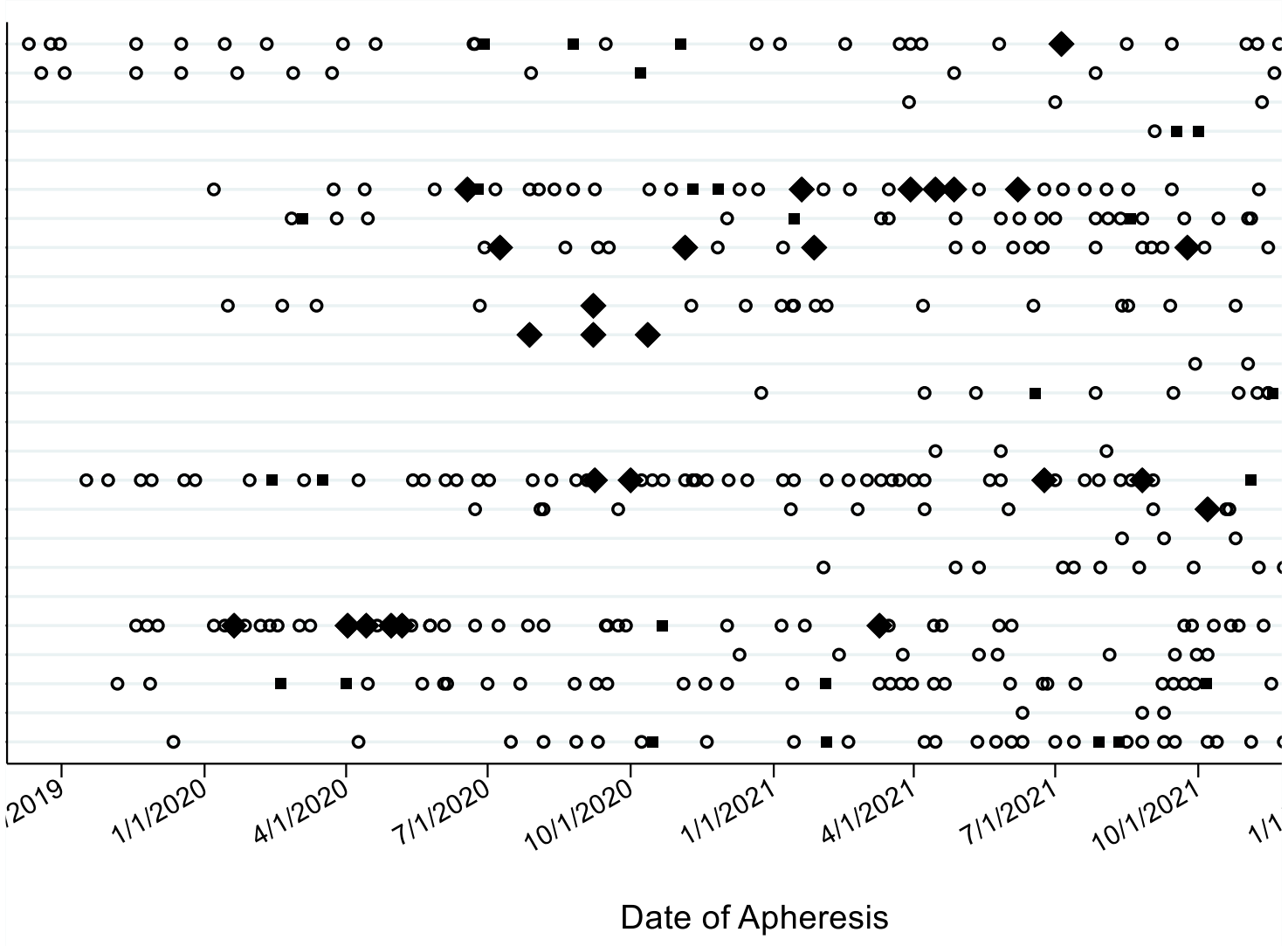
Success 77 cases
OOS 4 cases
Failure 0 cases



JSH（2022/11）/ 64th ASH Oral #664 / Jo T, Arai Y, et al British Journal of Hematology 2023 Scientifc Reports | (2023) 13:14952

Kymriah product score for 23 Japanese sites（DLBCL）

Facility



○ Success
■ OOS
◆ Failure

一般社団法人
日本輸血・細胞治療学会

委員会名： 免疫・再生医療関連委員会
ワーキンググループ(WG)・タスクフォース

manufacturing

23 sites
408 cases

Explore the factors that affect the success rate of CAR-T manufacturing

Patient episodes for success or failure of CAR-T therapy

Femail 20 s

- Primary mediastinal Large B cell lymphoma
- Treatment
  - DA-EPOCH-R 6 courses ：CR
  - Recurrence→R-ESHAP：no CR
  - R-GCD→Pola BR：no CR
  - **Apheresis →manufacturing OK**
  - IVAC→rediation：PR
  - **CAR-T：CR**
  - No event

Mail 60s

- Diffuse large B lymphoma
- Treatment
  - R-CHOP　1 course：PR
  - BR 4 courses：no CR
  - R-CHASE　1course：PR
  - **Apheresis→manufacturing failure**
  - R-CHASE　2 courses
  - **Apheresis 2→manufacturing failure again**

Additional chemotherapy is not feasible.

Pretreatment conditioning

Factors determine the success of CAR-T manufacturing

Bendamustine risk category High risk：> 3 courses, last Tx conducted within 3 M, Middle risk：> 6 courses last Tx conducted 3 after or within 24 M

		Odds ratio	95%CI	p value
Risk by Bendamustine	Low		Reference	
Pretreatment conditioning	Int	**5.520**	(1.436 - 21.215)	0.013*
	High	**57.088**	(3.370 - 966.996)	0.005*
Platelet	Every 10 × 10^4/μL reduction	**2.020**	(1.107 - 3.690)	0.022*
CD4/CD8 ratio	≥1/3		Reference	
	<1/3	**3.249**	(1.314 - 8.036)	0.011*

Interpretation

Case 1

- ✓ Bendamustine ：no use （Low）
- ✓ Platelet：20.0 X 10^4 /μL
- ✓ CD4/CD8 ratio: 1.0 （≥1/3）

Odds ratio

× 57.1
× 2.0
× 3.2
= X **365**

Case 2

- ✓ Bendmustine：6 cycles & rest 2 months （High）
- ✓ Platlet：10.0 X10^4/μL
- ✓ CD4/CD8 ratio: 0.2 （<1/3）

JSH（2022/11）/ 64th ASH Oral #664 Scientific Reports 2023 / Jo T, Arai Y, et al British Journal of Hematology 2023

How can we address manufacture related CQAs ?

Cell manufacturing is still not industrialized !

Complicated manual operation in cell processing center

Change clothes to dust-free wear

Wear gloves and mask

Change into clean shoes

Open culture system

Verify operator's performance with a checklist

Work in extremely uncomfortable clothing

A robot that copies or mimics manual operation would eliminate human error and certainly improve efficiency ...

However, a robot without a sensor and without a data collection function requires "verification" of the final product for each shipment.

Pharma 3.0

www/ indiantelevison.com

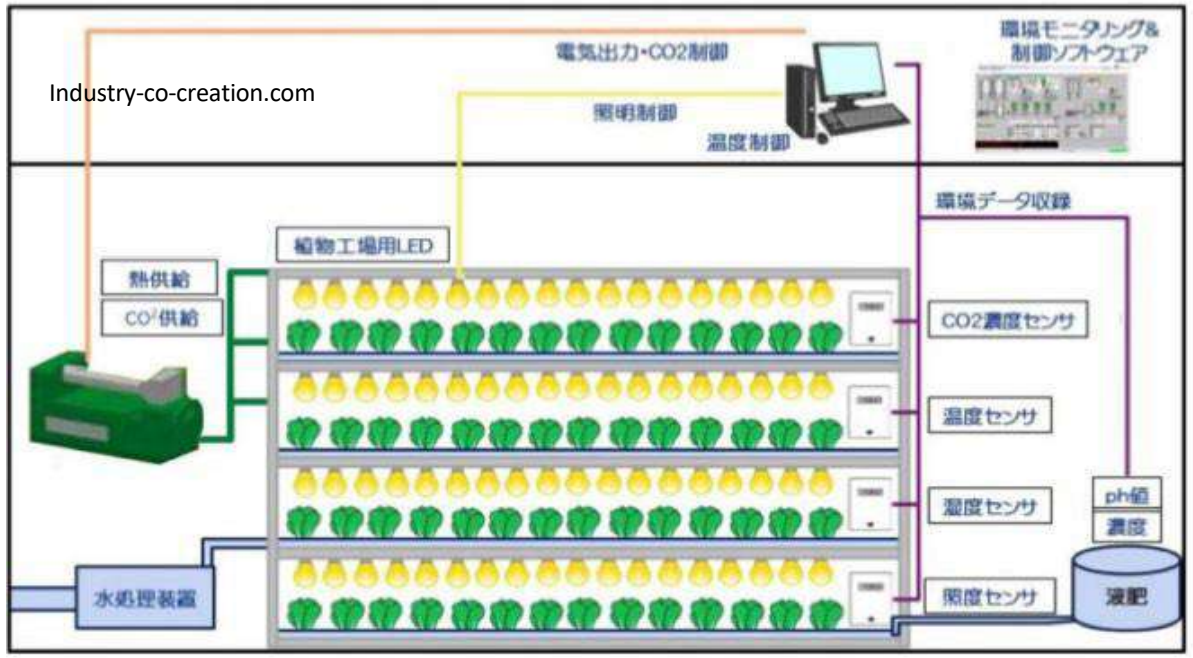
skipara.world press.com Kawasaki

How can we assure the quality of living materials, such as vegetables are manufactured as designed ?

First, the developer must have an image of the product with defined efficacy and then set up SOPs and process parameters (PPs) within the design space (DS). Next, confirm the quality of the product by ensuring the PPs are within the DS through in-process monitoring.

This is the Quality by Design (QbD)-based manufacturing.

Pharma 4.0



Aquaculture of Fugu is an example of Quality by Design (QbD)-based manufacturing

First, we need to have a clear image of Fugu with taste. Second, set up SOP to aquaculture Fugu from fry of heterogenous in size, and set up PPs and DS along with PPs. Then, confirm that tasty Fugu is aquacultured as designed without easting by confirming PPs are within DS.

Fry are heterogeneous in size

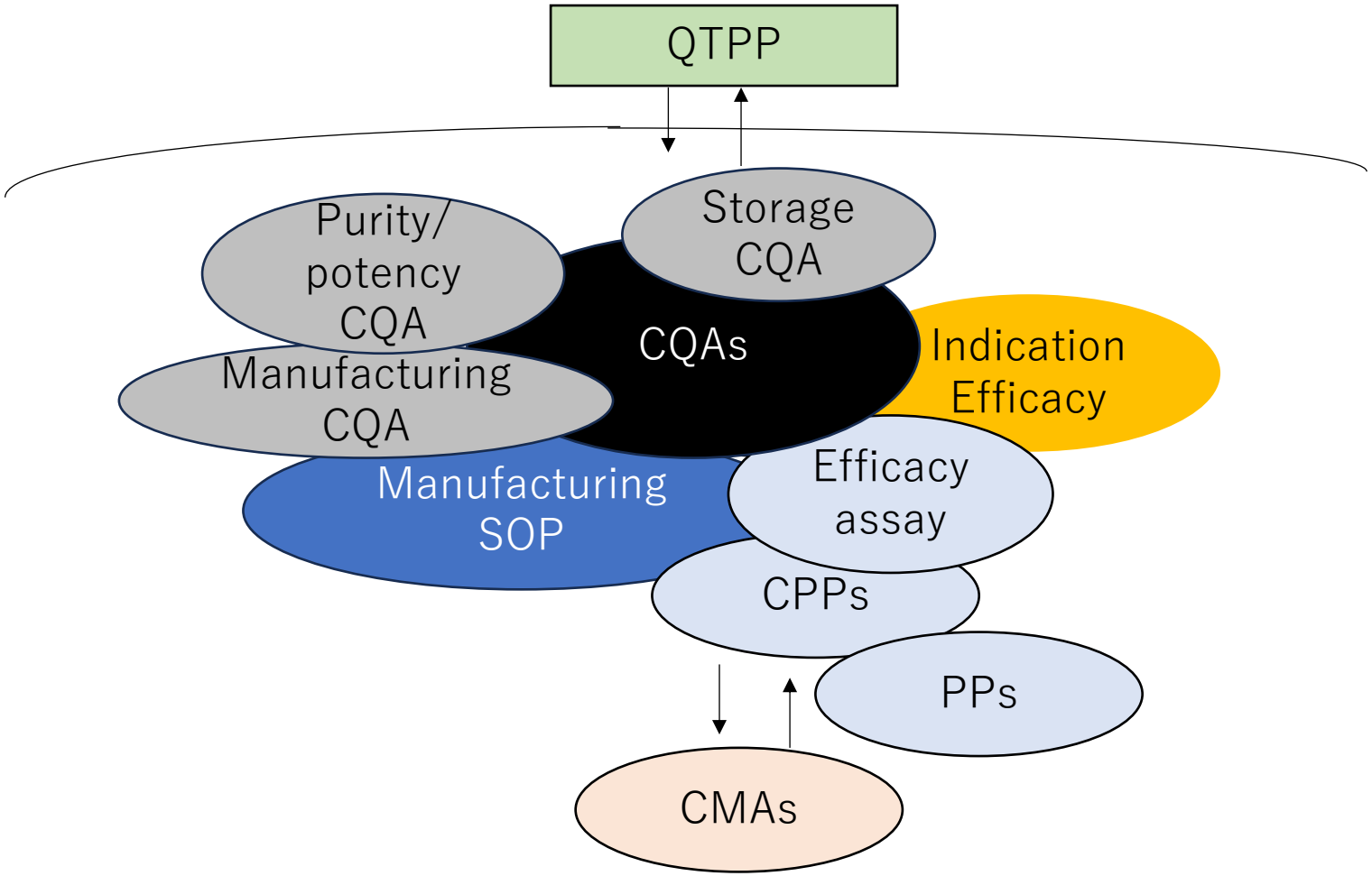
Delicious Fugu in 1.5-2.0 years

Manufacturing control of aquaculture of Fugu

Guarantee the same good taste without eating

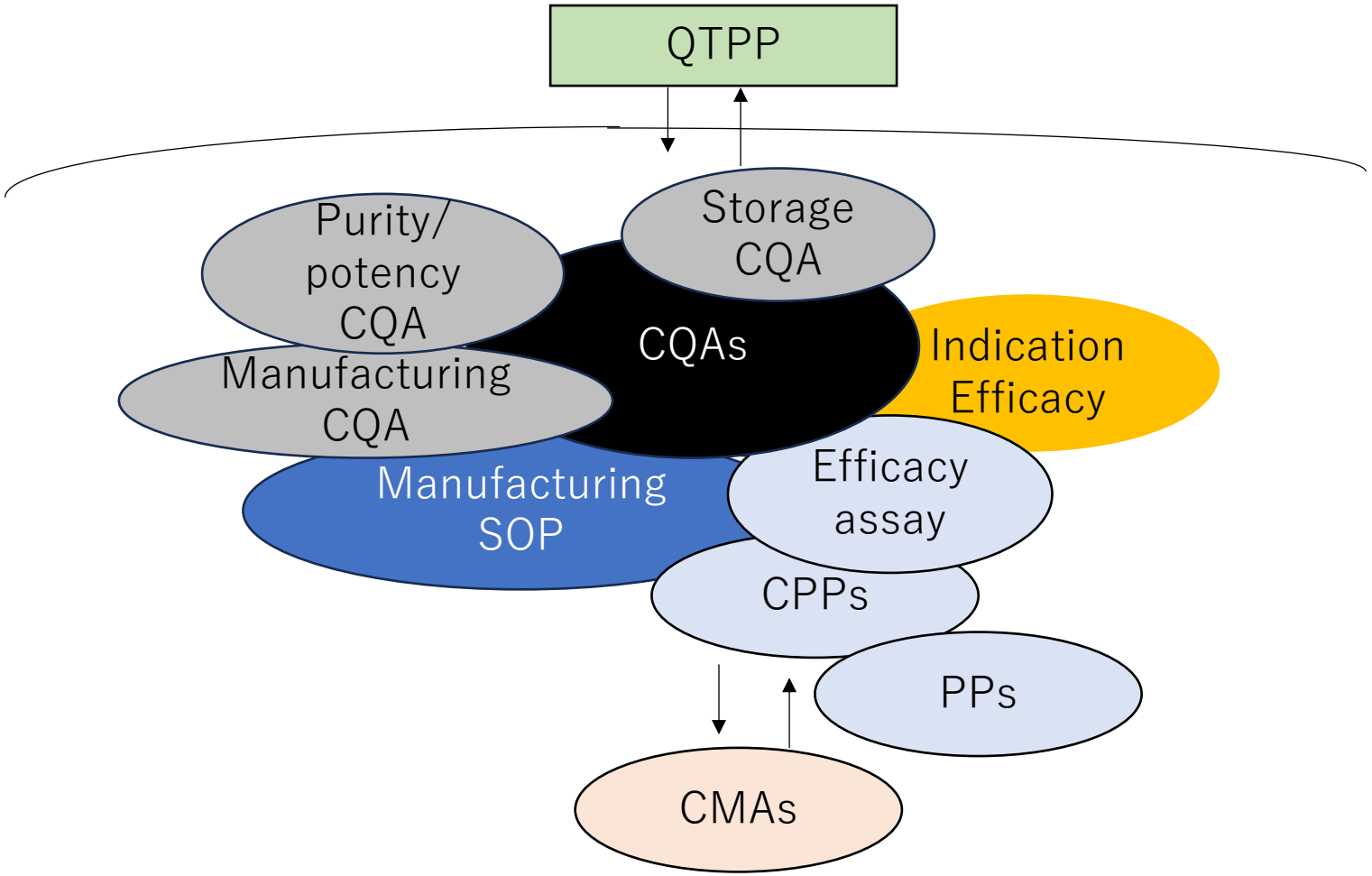
Process record obtained by in-process monitoring is batch record for release.

Schema for Quality by Design (QbD)-base manufacturing



Then, how can we set up PPs for MSC?

First, we need to define efficacy of the product.
In this case, efficacy of MSC is defined as anti-inflammatory effect.



Schema for MSC: mesenchymal stem cells in culture

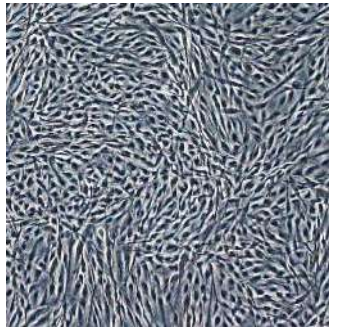
Heterogenous in shape and proliferation potential, but maintain constancy as a population until certain passages

Passage number

P3

P5

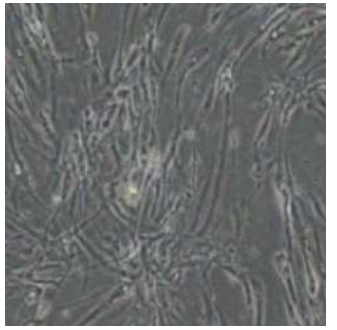
P7



Early passages **maintain** constancy (no-aged)

P9

P11

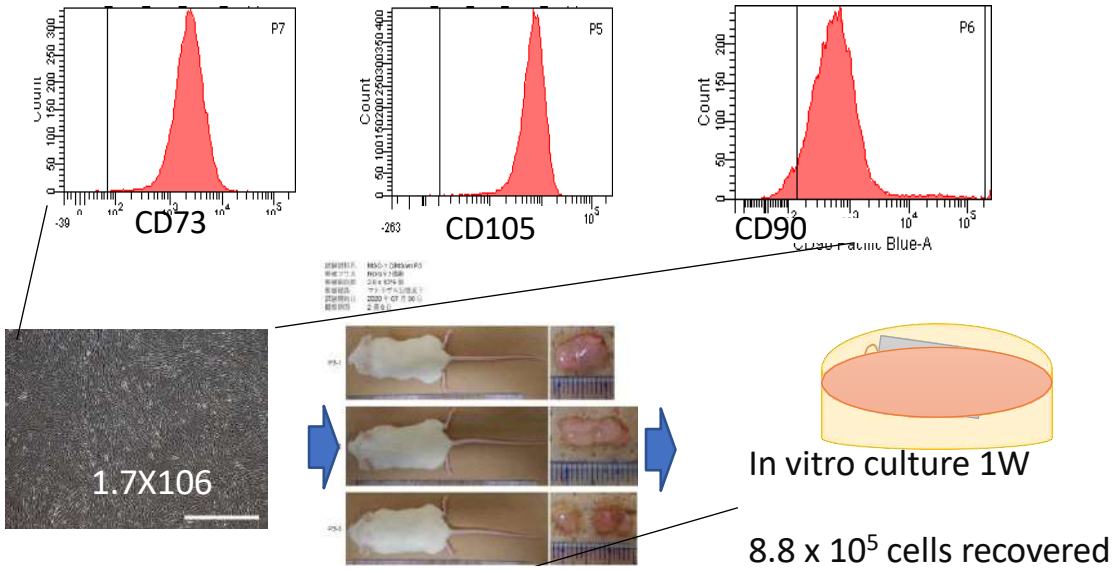


Late passages **lost** constancy (aged)

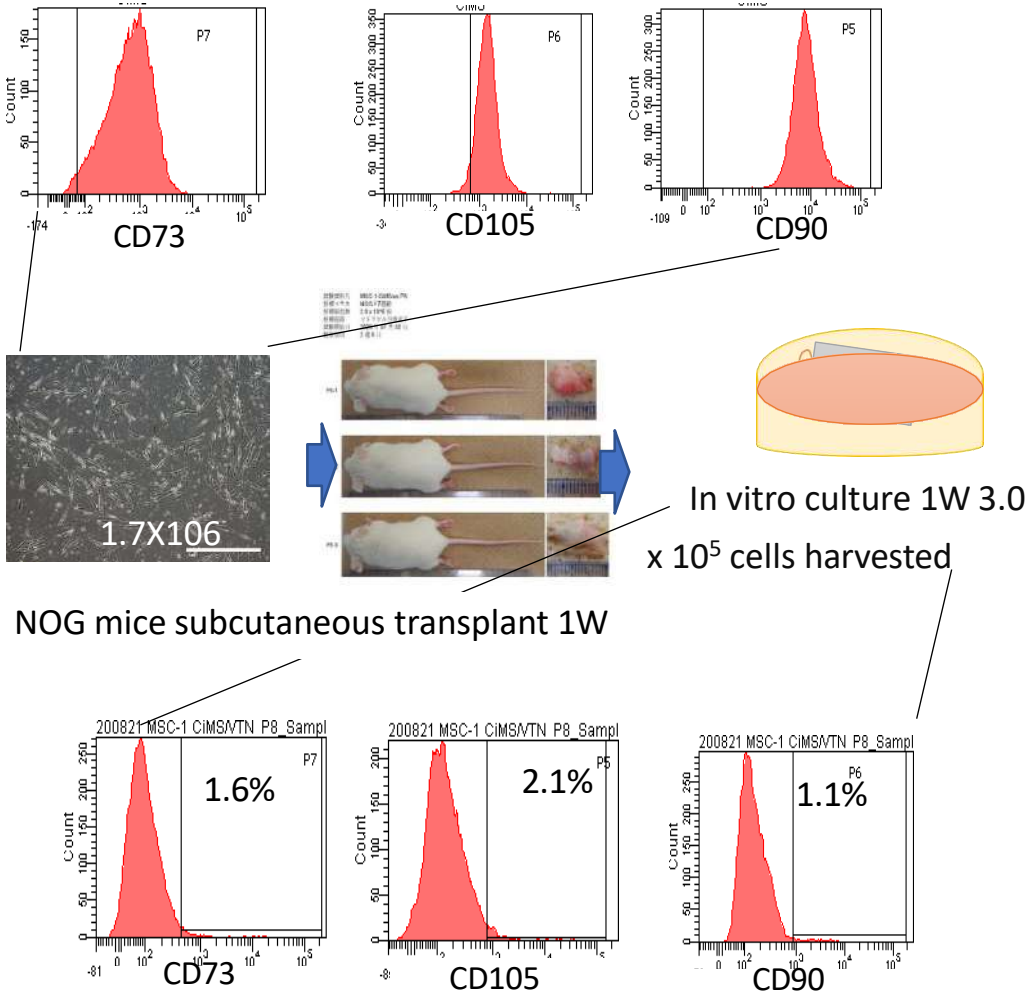
Is there any pharmaceutical difference between no-aged and aged population?

Yes, MSC with early passages may retain pharmaceutical potential, whereas late passages may not. ⇒ need to determine the permissible passage number that maintains pharmaceutical potential.

P3 (stem cells) CiMS MSC-1



P8 (non-stem cells) CiMS MSC-1

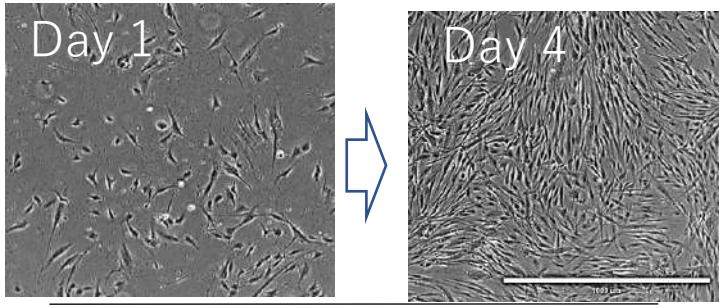


However, MSCs stop growing in late passages regardless of medium or cell source

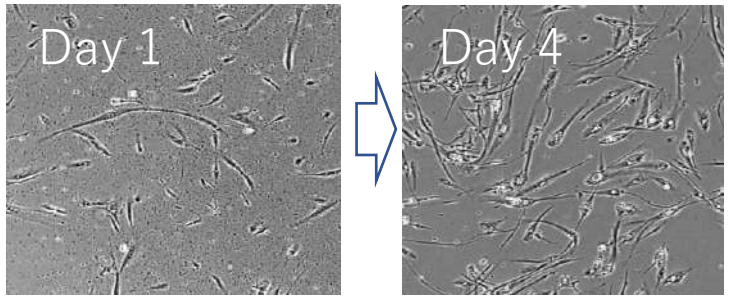
Non-attenuating cell growth in early passage can be a characteristic feature of all MSCs

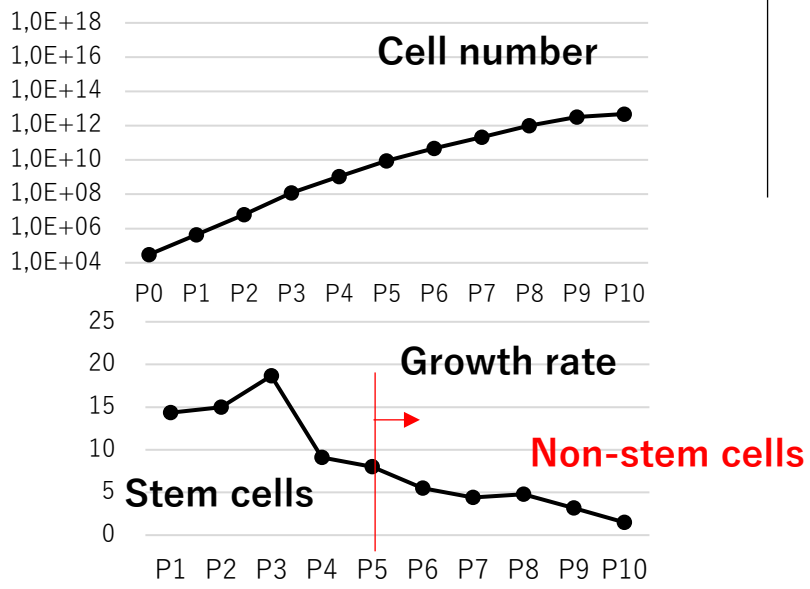
CiMS

P3



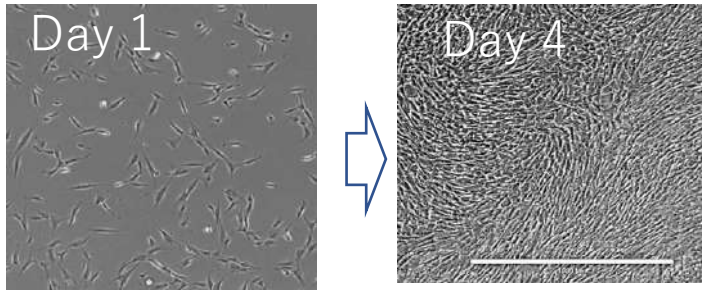
P8



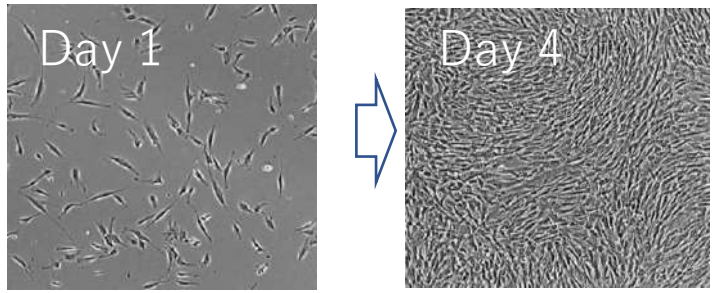


Cellartis

P3

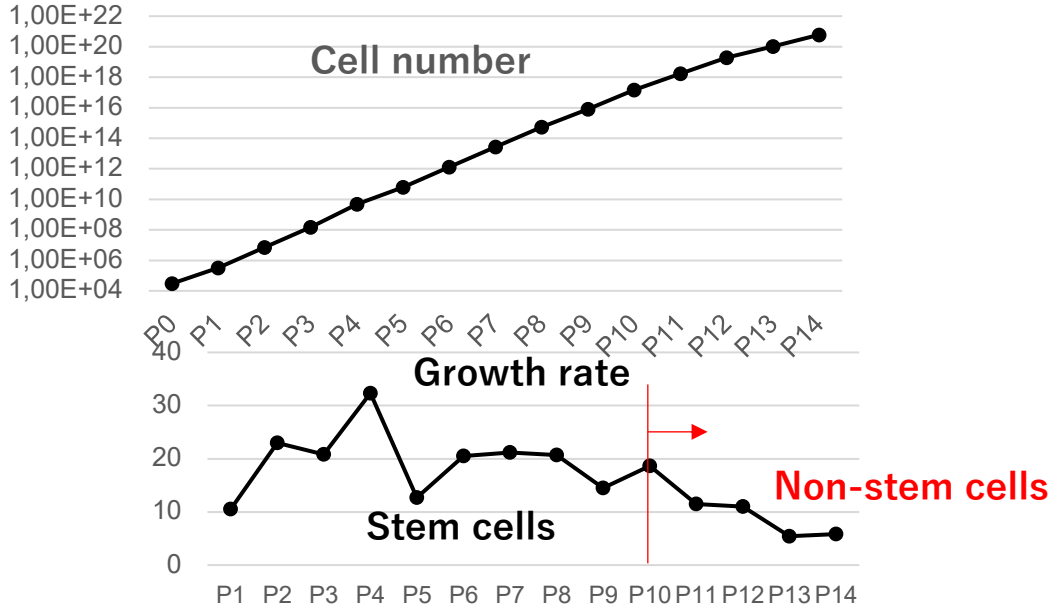


P8

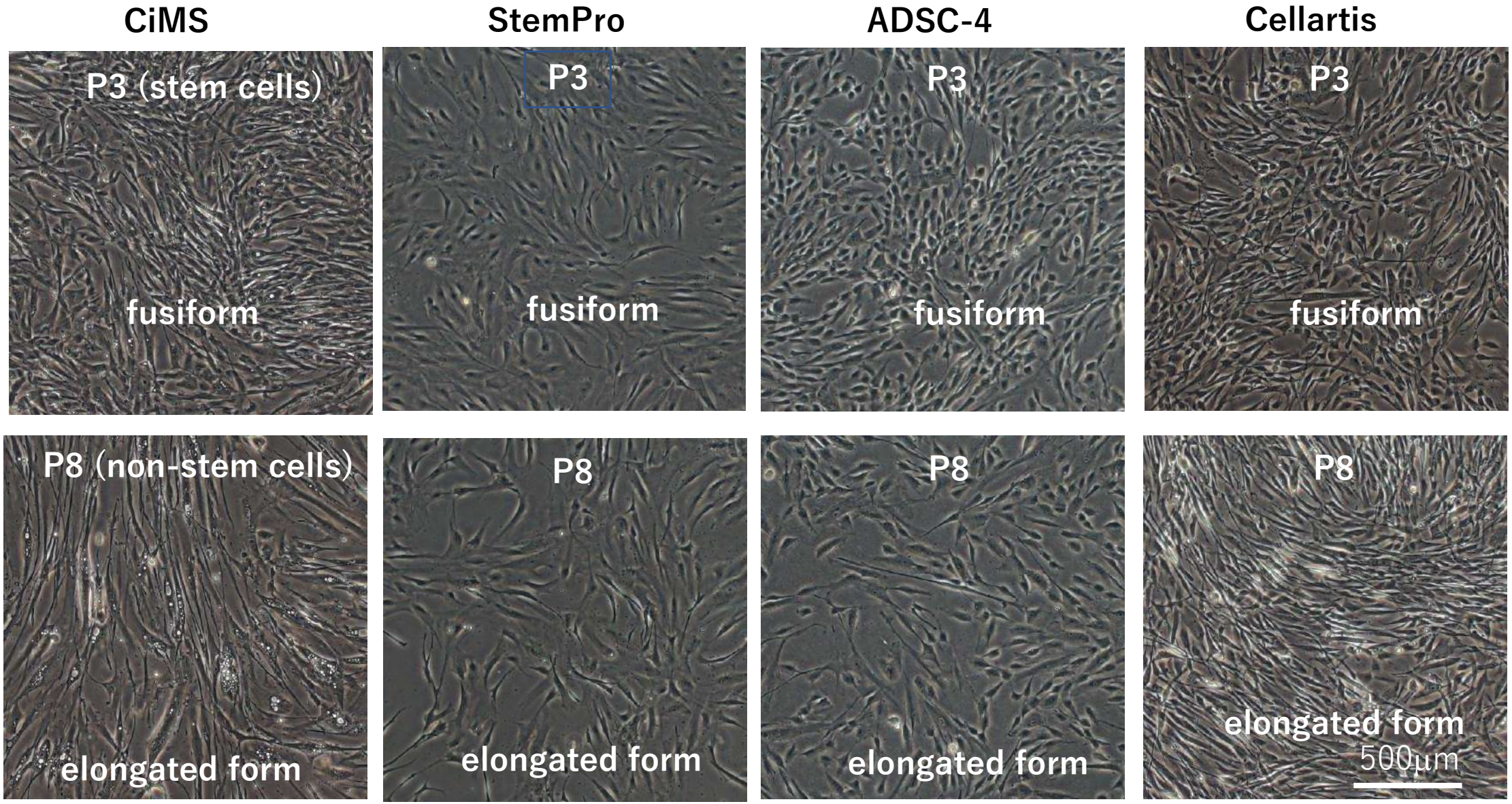


Stem cell population:
Cell population retains self-renewal potential

Non-stem cell population:
Cell population losses self-renewal potential



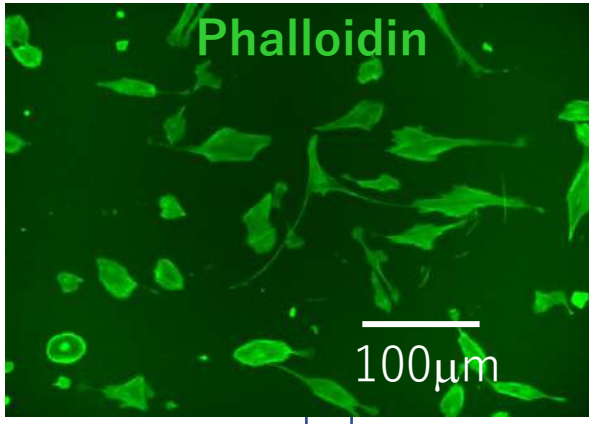
Cell morphology in early passages may differ from that in late passages.
⇒Cell morphology can be a process parameter (PP) to harvest the target cells



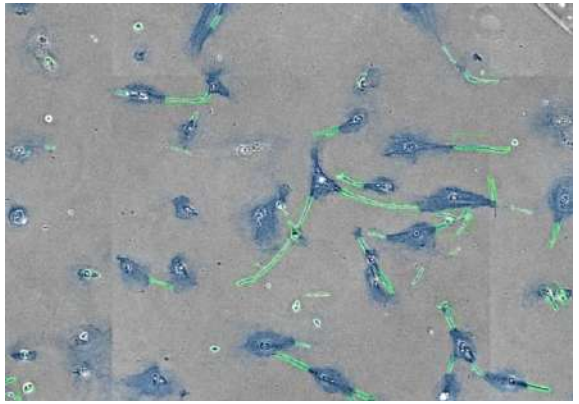
MSC-4 (adipocyte origin)

Cell morphology defined by area of pseudopods with AI can be a PP

Cell pocket　Shimadzu



Detection of pseudopods



Yamamoto Stem Cell Translational Medicine 2023

MSC-1　CiMS

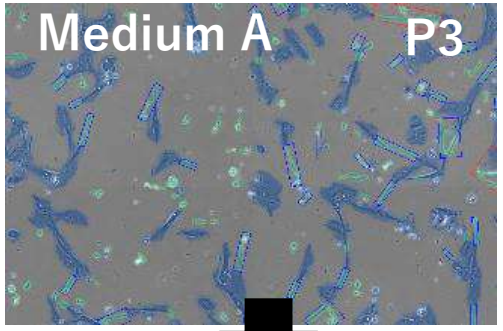
Retain Homeostatic feature

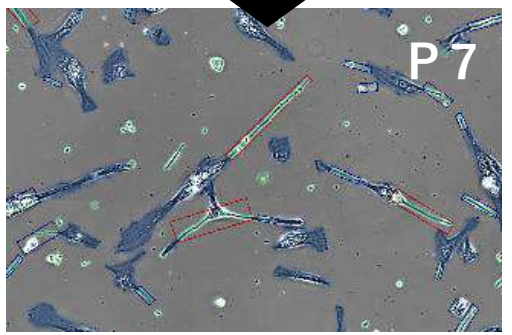
Target (stem cells)

off-target (non-stem cells)

Loss Homeostatic feature

Passage number	%
	MSC-1
3	3.2
4	3.8
5	3.8
6	5.7
7	6.8
8	8.8
9	9.7
10	10.7





MSC-1　Cellartis

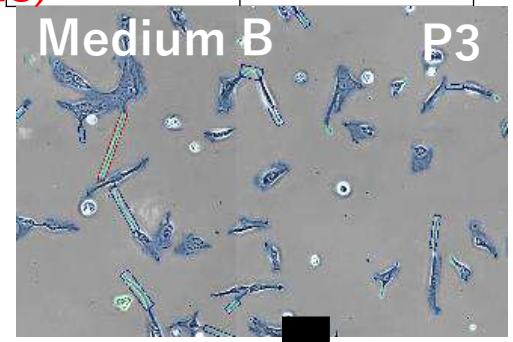
Retain Homeostatic feature

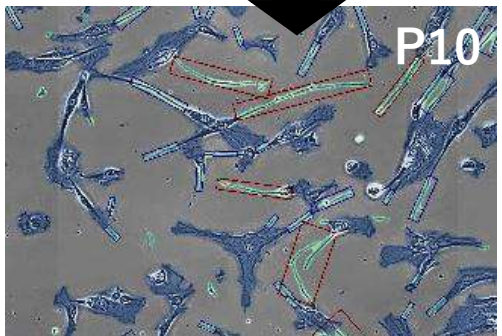
Target (stem cells)

off-target (non-stem cells)

Loss Homeostatic feature

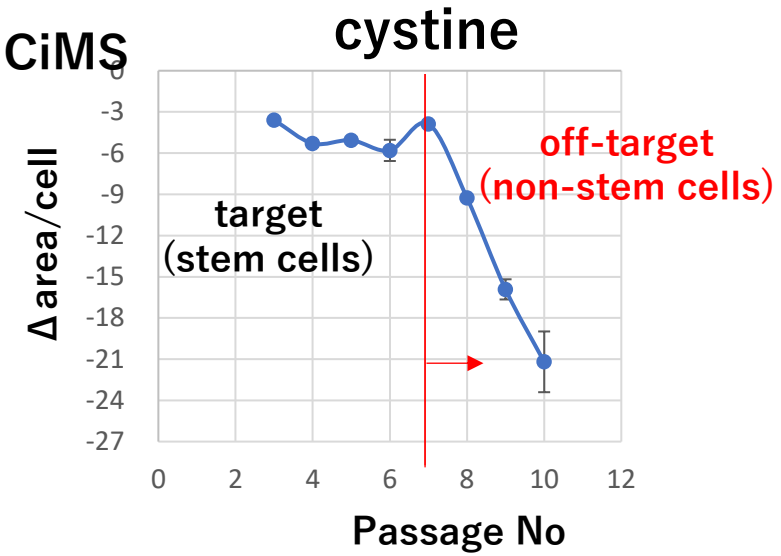
Passage number	%
	MSC-1
3	2.9
4	3.4
5	3.5
6	4.0
7	4.0
8	5.4
9	10.7
10	11.2

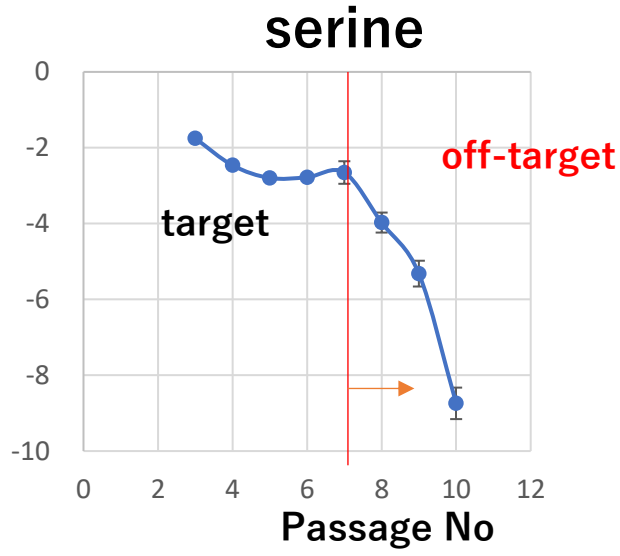




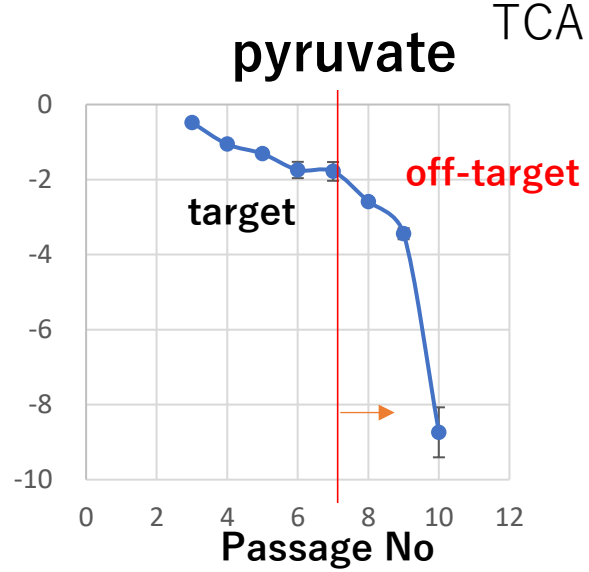
Quantitative analysis of reluctant consumption in medium can be a PP

MSC-1 CiMS

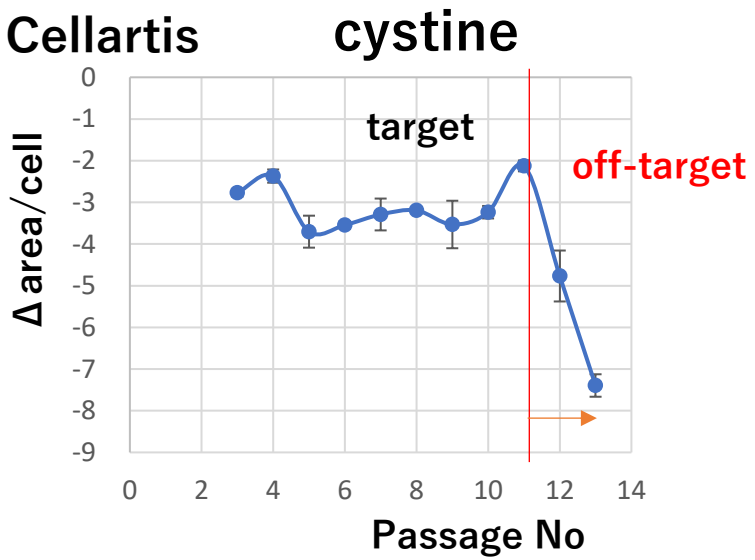


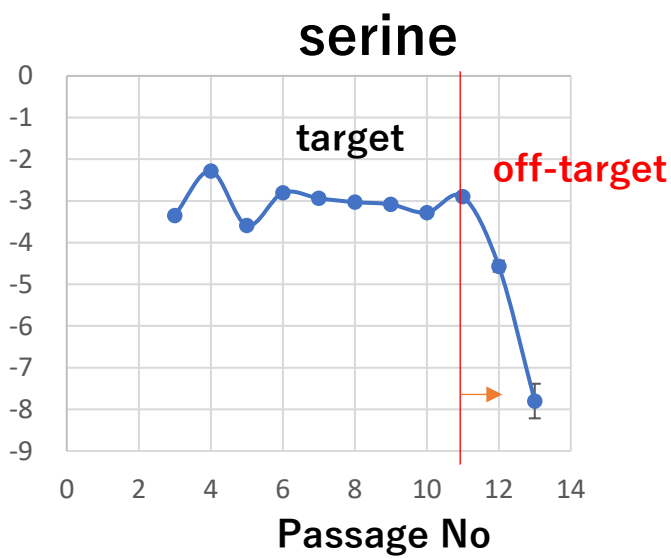


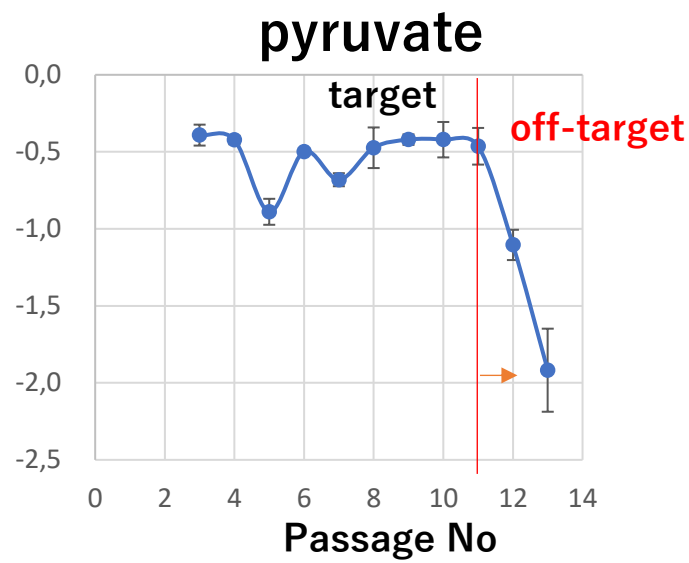
TCA cycle



MSC-1 Cellartis



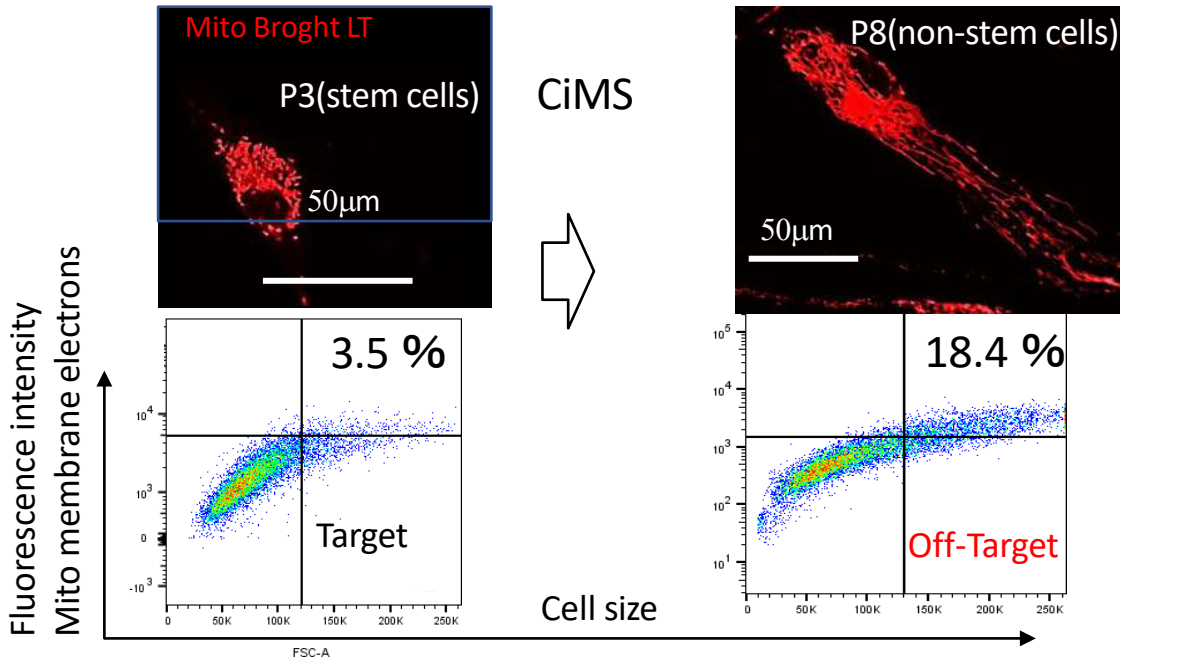


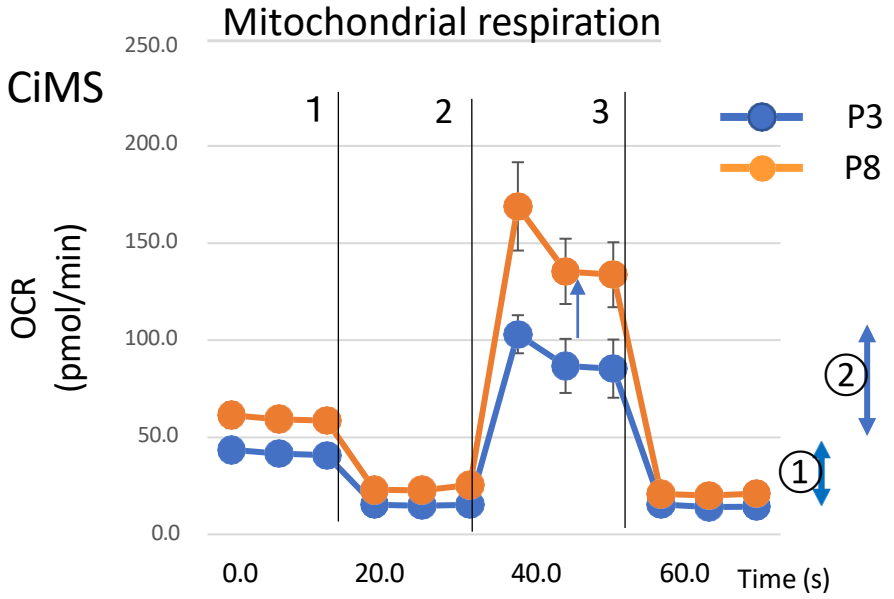


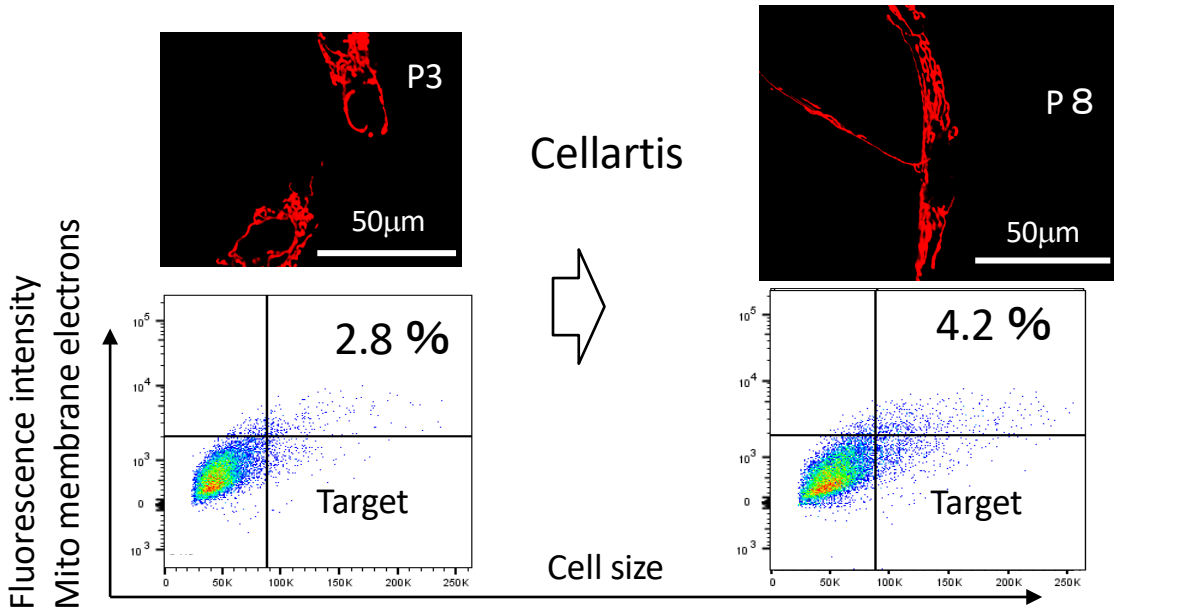
Δarea/cell: **area of the analyte peak of the relevant amino acid by LC-Mass for its quantification /single cell**

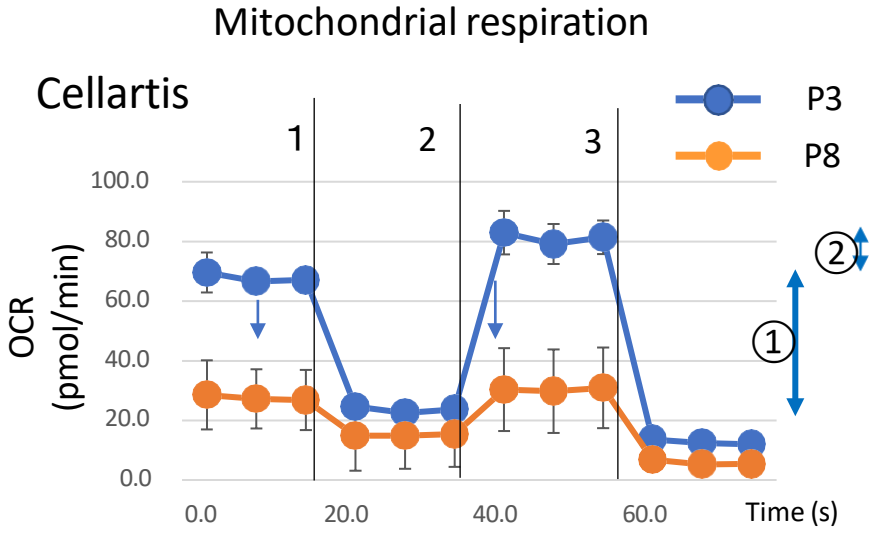
Yamamoto Stem Cell Translational Medicine 2023

Deterioration of mitochondria is medium type and passage number dependent



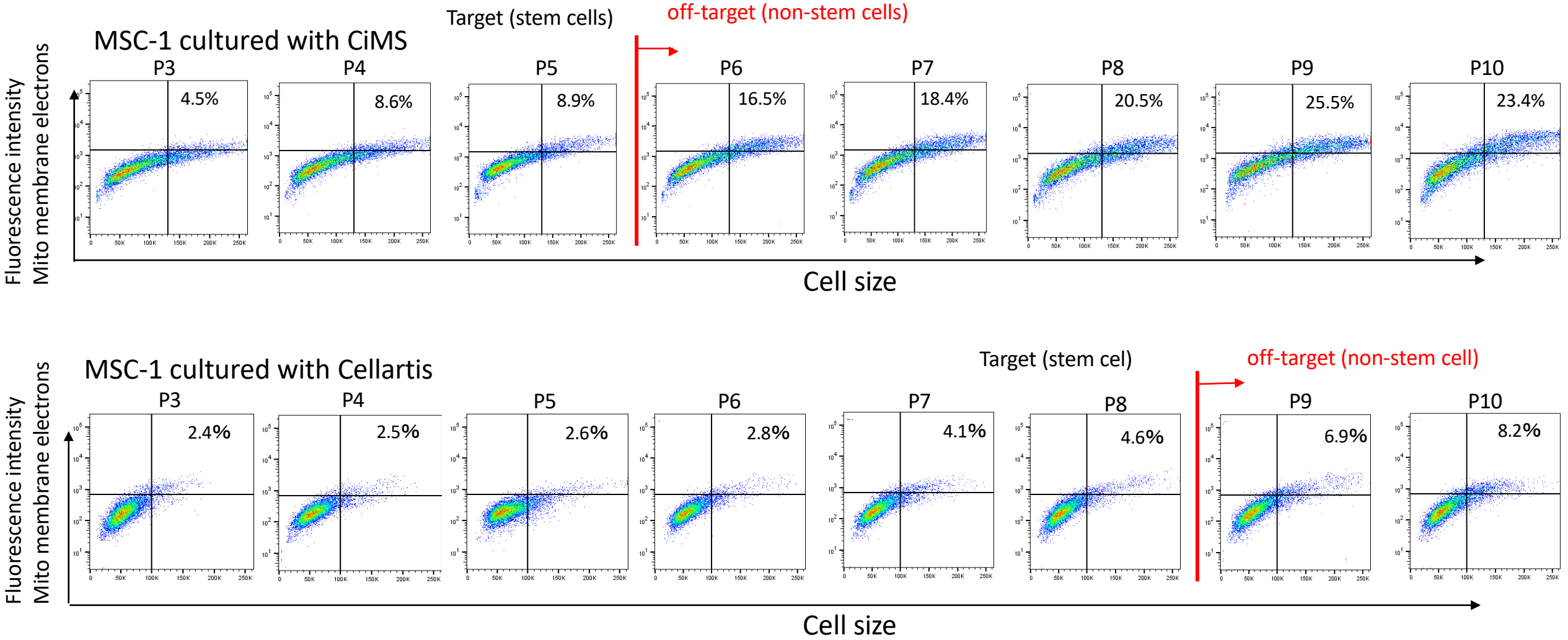






Yamamoto Stem Cell Translational Medicine 2023

Mitochondrial size measured by membrane electrons and size of MSCs can be critical PP for harvesting target cells



Yamamoto Stem Cell Translational Medicine 2023

PPs that can define the CQAs related manufacturing of MSC

Process parameters （PPs) and their tentative control values that enable to harvest cells retaining self-renewal potential

	CiMS	Cellartis
No reduction of cell growth： growth rate ＞ X 10	P＜ 6	P≦10
Retain homogenous cell morphology：Psuedopods ≦5.4%	P<5	P≦11
Retain Redox balance：cystine consumption ≧ -3, serine consumption ≧ -3 △area/cell	P<7	P≦11
Retain TCA cycle activity ：pyruvate consumption ≧ -1.0 △area/cell	P<7	P≦11
No mitochondrial deterioration by ROS： membrane bound electron/cell size ≦ 4.6%	P<5	P≦8

CPP

Anti inflammatory potency of cells harvested with PPs

IL-6 PBMC co-culture with MSC 24 h and 72 h 20 ng/mL

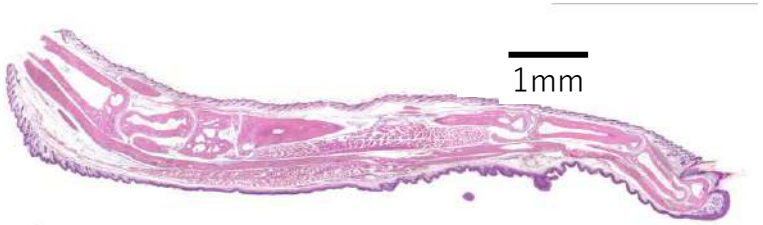
IL-10 PBMC co-culture with MSC 24 h and 72 h 1.0 ng/mL

Treg induction at 72 h from PBMC co-culture with MSC ＞ 5.0 %

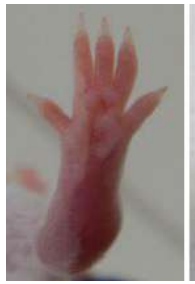
Efficacy of cells harvested with stipulated PPs can be verified in vivo, which in turn serves as validation of the stipulated PPs.

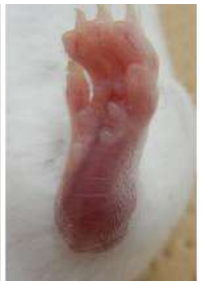
Harvest cells by PPs⇒check validity of cells harvested by PPs *in vivo* ⇒ check validity of stimulated PPs⇒determination of CPPs and CQAs

Non treated（SKG mouse）



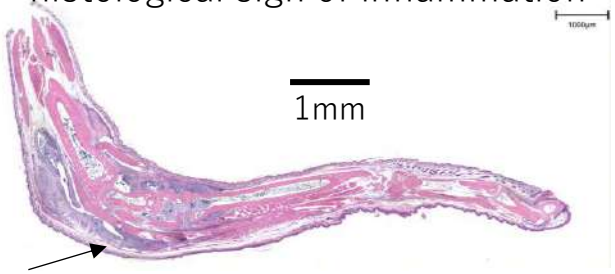
PBS



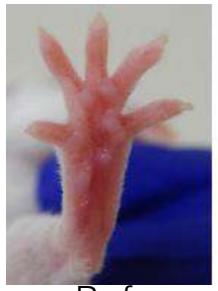


Before　After iv

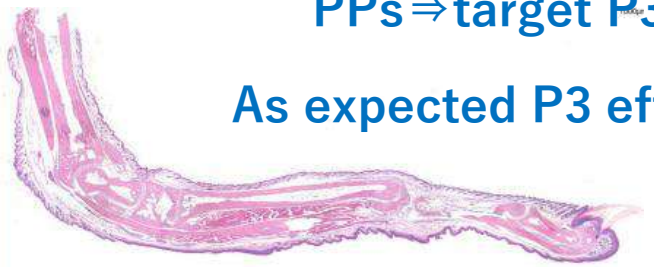
IHC for CD4+ cells
histological sign of inflammation



CiMS P3 (target cells)



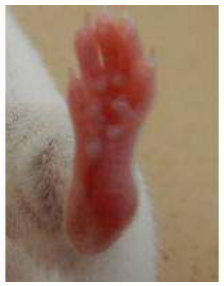
Before　After iv



PPs⇒target P3-P5

As expected P3 effective

Cellartis P3 (target cells)

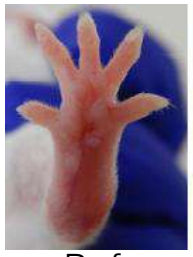


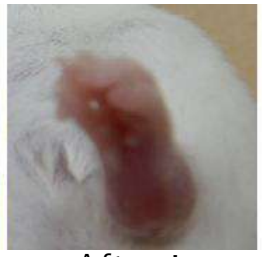
Before　After iv

PPs⇒target P3- 8

As expected P3 effective

CiMS P8 (off-target cells)





Before　After iv

As expected P8 not effective

IHC for CD4+ cells
histological sign of inflammation

Cellartis P8 (target cells)

Before　After iv

As expected P8 effective

Yamamoto Stem Cell Translational Medicine 2023

Automated cell manufacturing system with in-process monitoring that realizes QbD-based manufacturing

Intelligent Cell Processing System

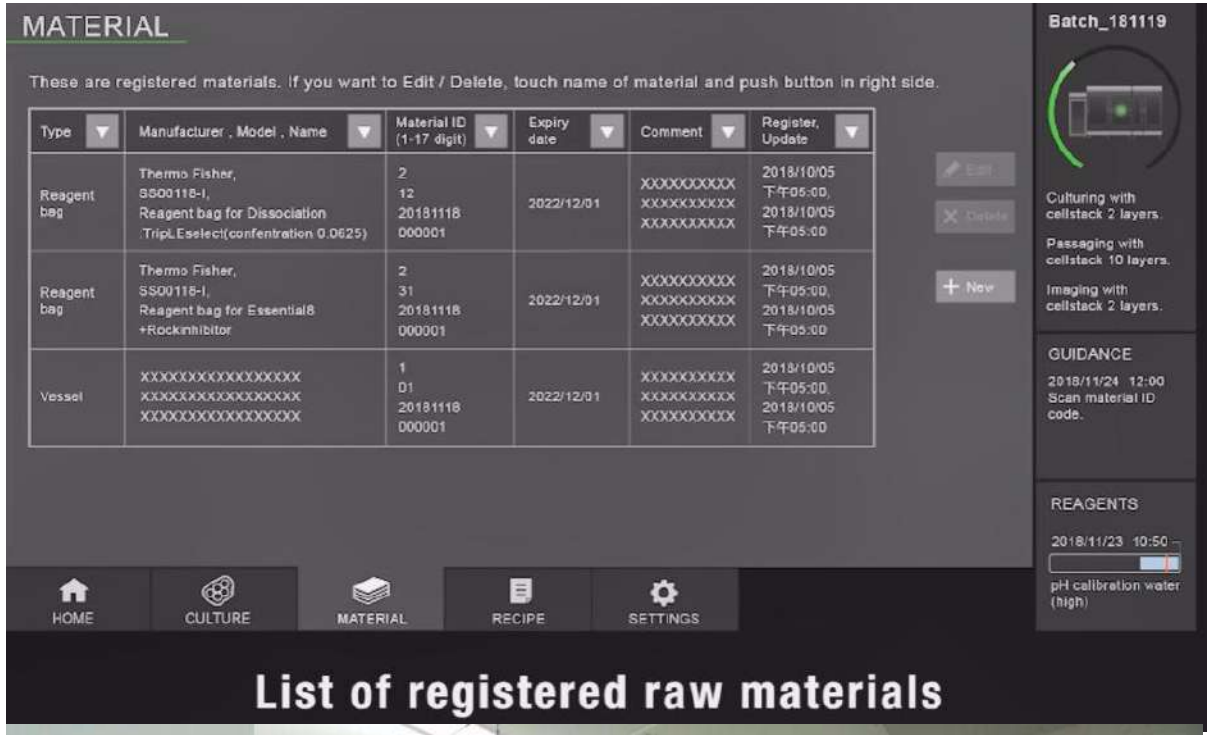
SINFONIA

Refrigerator module

Incubation module

- ✓ Closed automated culture system
- ✓ Real-time vision tool
- ✓ In process medium analysis
- ✓ Auto sampling for off-line QC
- ✓ Manufacturing data in IT format

Registration of raw materials

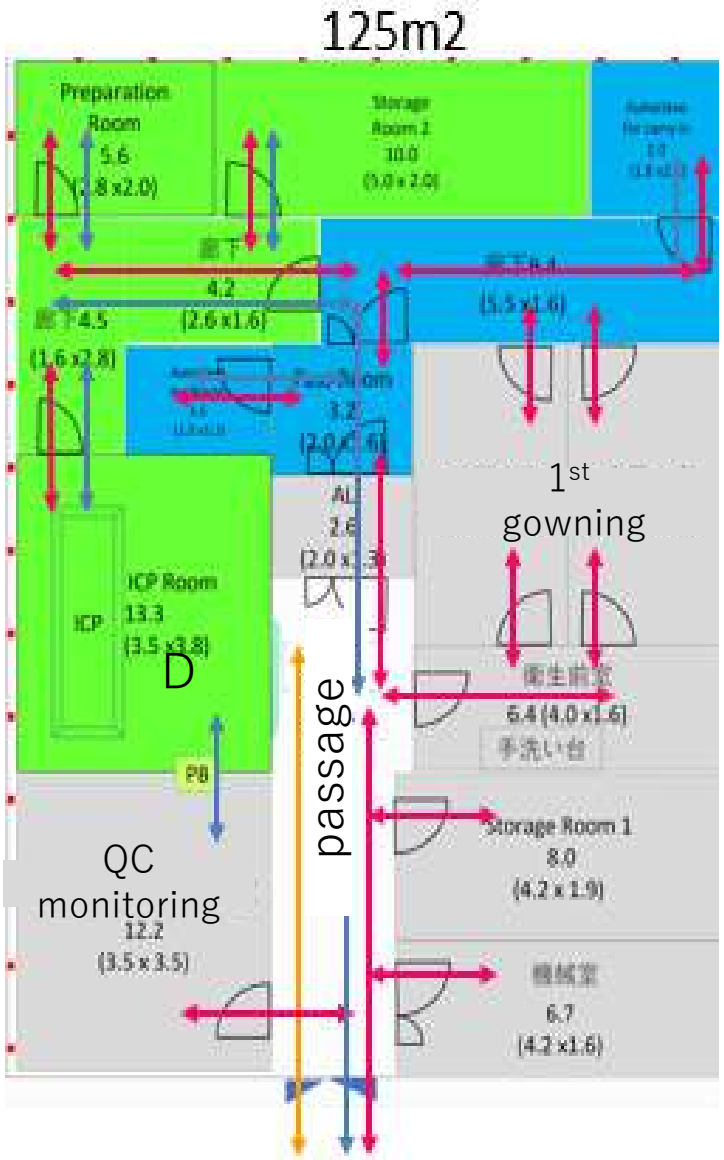


List of registered raw materials

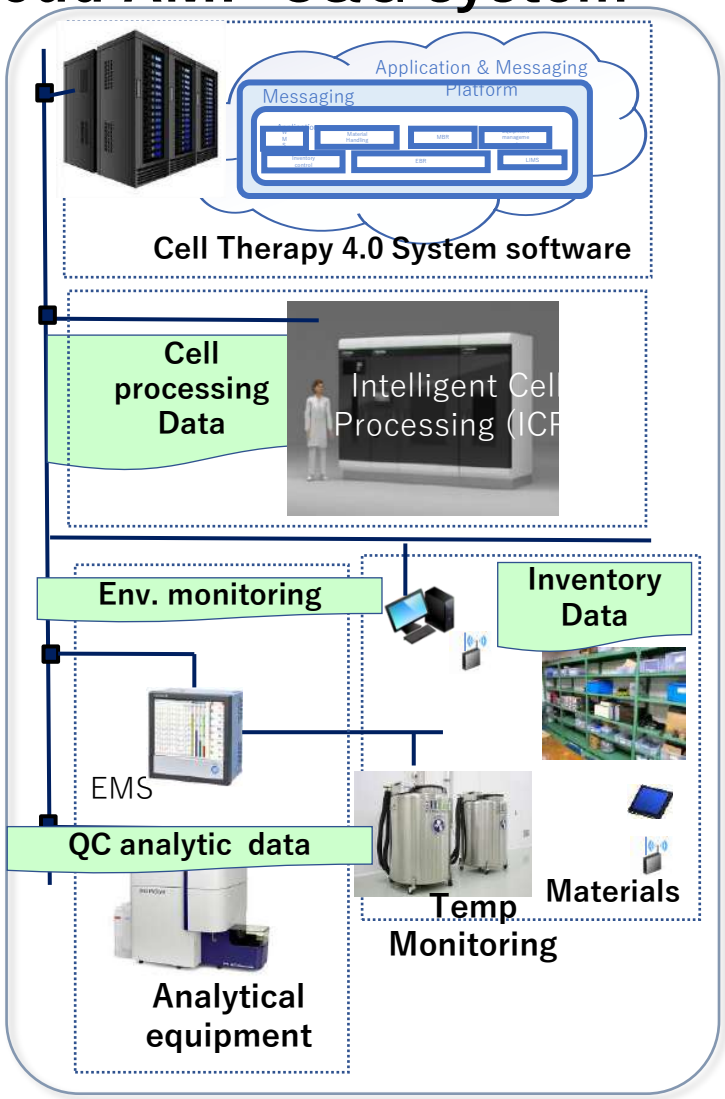
Installation of fully closed cell culture unit

Setting culture parameters and instrument functions

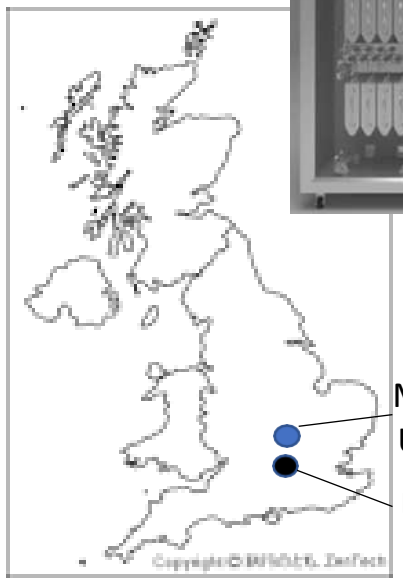
KCMI in Kobe show room
QbD-based cell manufacture and trial manufacturing

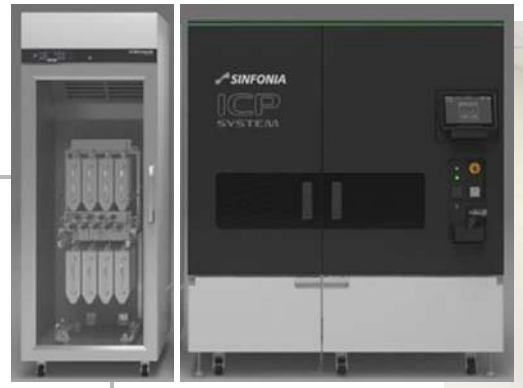


Cloud AMP C&G system



The QbD-based automated cell manufacturing system CellQualia was evaluated by UK Stem Cell MHRA, a mirror image experiment





Patters Bar
MHRA NIBSC
UK Stem Cell

London

Kobe
KCMI

Comparability test

MHRA trialling pioneering stem cell robot that could transform the availability of life-saving cell therapies - GOV.UK (www.gov.uk)<https://www.gov.uk/government/news/mhra-trialling-pioneering-stem-cell-robot-that-could-transform-the-availability-of-life-saving-cell-therapies>

Automated closed cell manufacturing system CellQualia was highly rated by MHRA, UK Government

https://www.gov.uk/government/news/mhra-trialling-pioneering-stem-cell-robot-that-could-transform-the-availability-of-life-saving-cell-therapies

March 16, 2023

GOV.UK

Home > Health and social care > Medicines, medical devices

Press release

MHRA trialling pioneering stem cell robot that could transform the availability of life-saving cell therapies

The MHRA's UK Stem Cell Bank is one of only two places in the world to test this technology.

From: Medicines and Healthcare products Regulatory Agency, Department of Health and Social Care, and The Rt Hon Steve Barclay MP

Published 16 March 2023

SINFONIA

Cyto-Facto

An innovative new robot that grows stem cells, the CellQualia™ Intelligent Cell Processing System, is being trialled by the Medicines and Healthcare products Regulatory Agency (MHRA). This robotic system has the potential to bring safer and more cost-effective treatments to people with a wide range of diseases. It is currently the only one in the world outside of Japan, where it was developed.

This trial is part of a UK-based international research programme, launched in 2021, and a partnership between the MHRA, SAKARTA (a Scottish Regenerative Medicine start-up), and Sinfonia Technology Co. Ltd (a Tokyo-based electrical equipment manufacturer), supported by Foundation for Biomedical Research and Innovation at Kobe (FBRI). The UK Stem Cell Bank is testing the robot over a 12-month period to see whether the cells produced by the fully automated Intelligent Cell Processing System meet the standards needed for them to be used in the manufacture of potentially life-saving treatments.

Example of eBatch record for MSC manufacturing

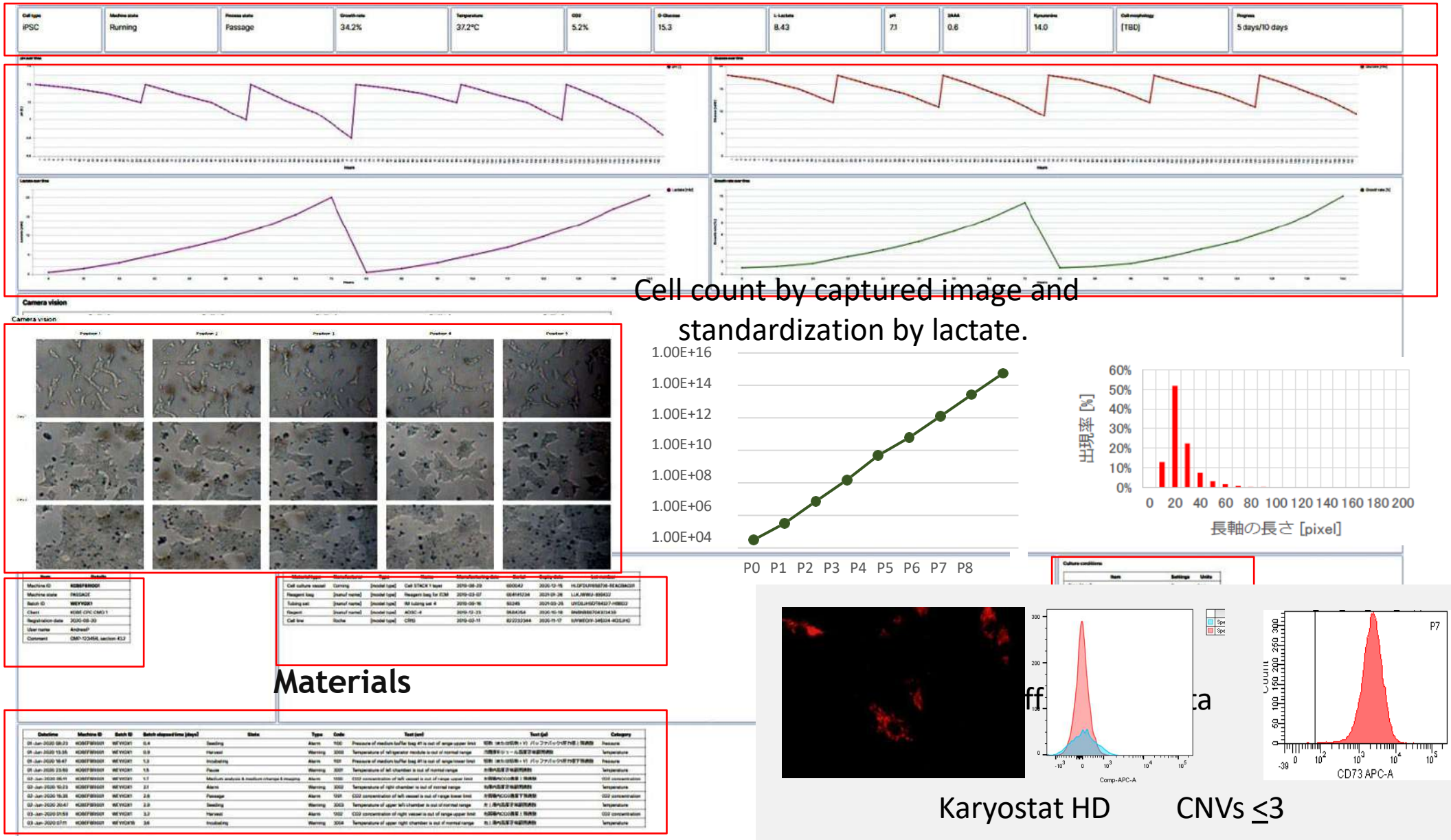
Status

In-line sensor pH, Glu, Lac, CO2

Cell image

Batch overview

Event log



Automated cell manufacturing award (2023)　UK

RegMedNet　Home　Journal　News　Topics　Features　Multimedia　Fi

Developing cell therapies with a stem cell robot

The UK was the second country to trial a pioneering stem cell robot to improve the manufacture of safe and cost-effective cell-based therapeutics. The CellQualia™ Intelligent Cell Processing System, which was developed in Japan, automates the culturing of cells in real time and stabilizes the process by utilizing intelligent process analytical technology.

https://www.regmednet.com/regmednets-2023-remix-top-content-of-the-year/

Automated cell manufacturing award (2024)　Japan

NIKKEI
日経優秀製品・サービス賞
2024

2024年で43回目を迎えた「日経優秀製品・サービス賞」では、グローバル市場に挑戦する製品・サービスが目立った。あらゆる分野で課題となっている人手不足に対応するものも多く、医療や宇宙など先端分野に自社で培った技術を応用する地域企業も存在感を示した。

生産財

自動細胞培養装置「CellQualia」

シンフォニアテクノロジー

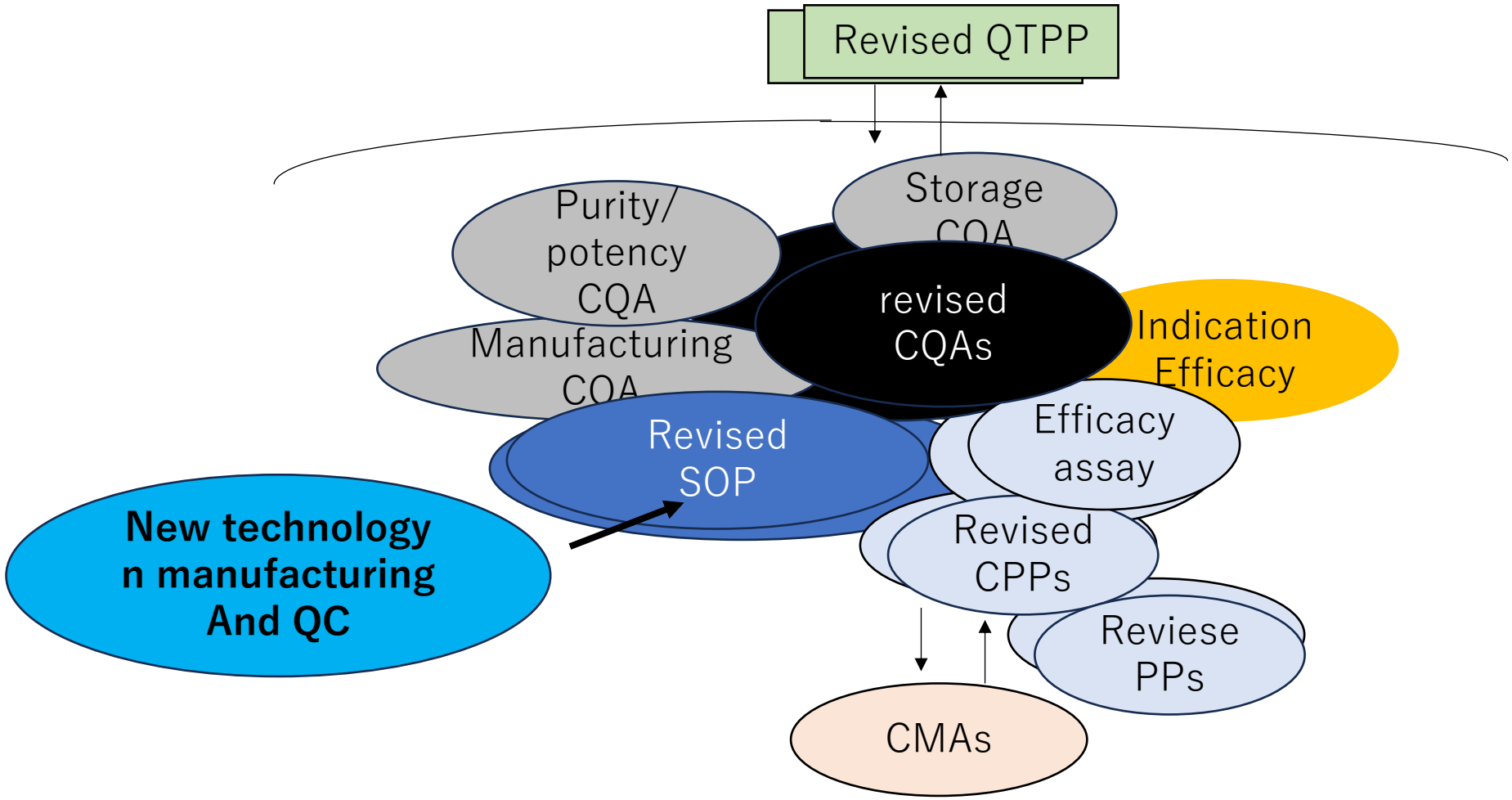
密閉型の自動細胞培養装置。神戸大学の川真田伸特命教授と共同で開発した。人体の組織や臓器を再生して体内に移植する再生医療ではあらゆる細胞に分化するiPS細胞の活用に期待が高まっている。ただ、高品質な細胞の大量生産が課題になっている。

新装置は細胞培養の工程を密閉された機器内で自動で繰り返す。培養データを常に監視しているため、細胞の品質も担保できる。培養後の検査などのコストを少なくできるといった利点がある。

細胞培養は通常、タネとなる細胞を培地にまいて増やしより大きな培地に移し替え、さらに増やす工程を繰り返す。手作業では技術者の練度に左右される。できあがった細胞に雑菌が混じっていないかの検査も必要になっている。

https://www.nikkei.com/edit/news/special/newpro/2024/

How can the life cycle development of a product be achieved through a QbD-based approach?

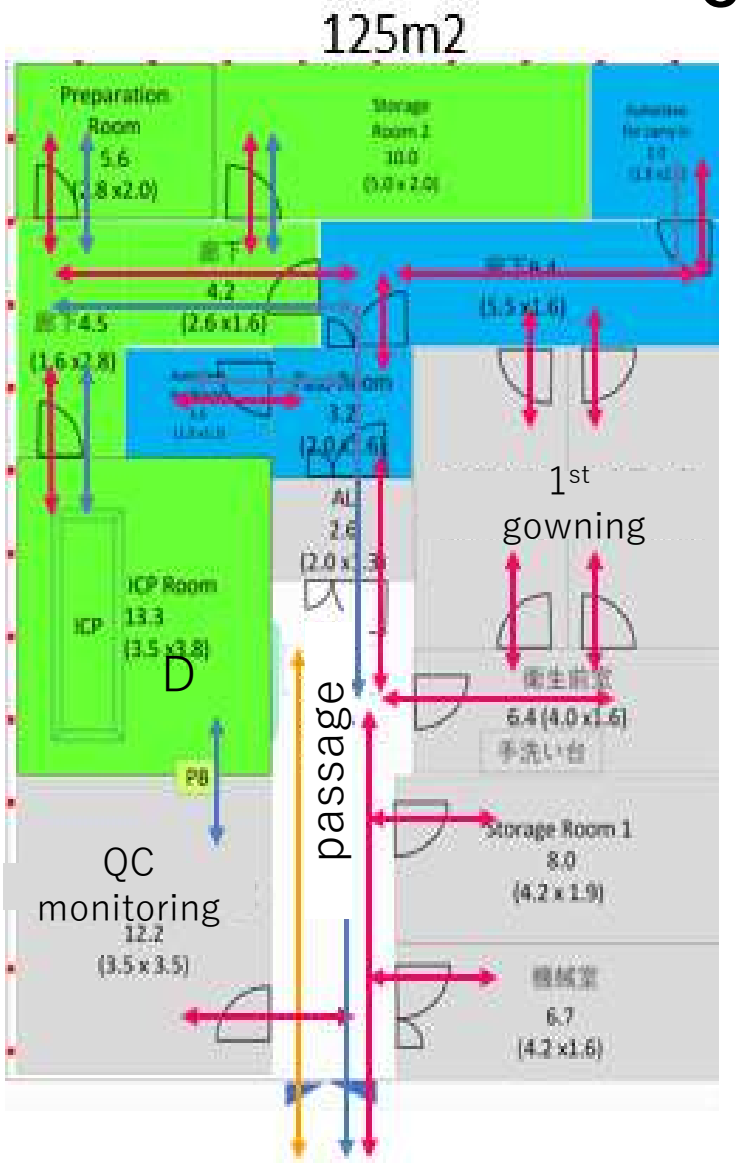


How does QbD-based manufacturing become feasible ?

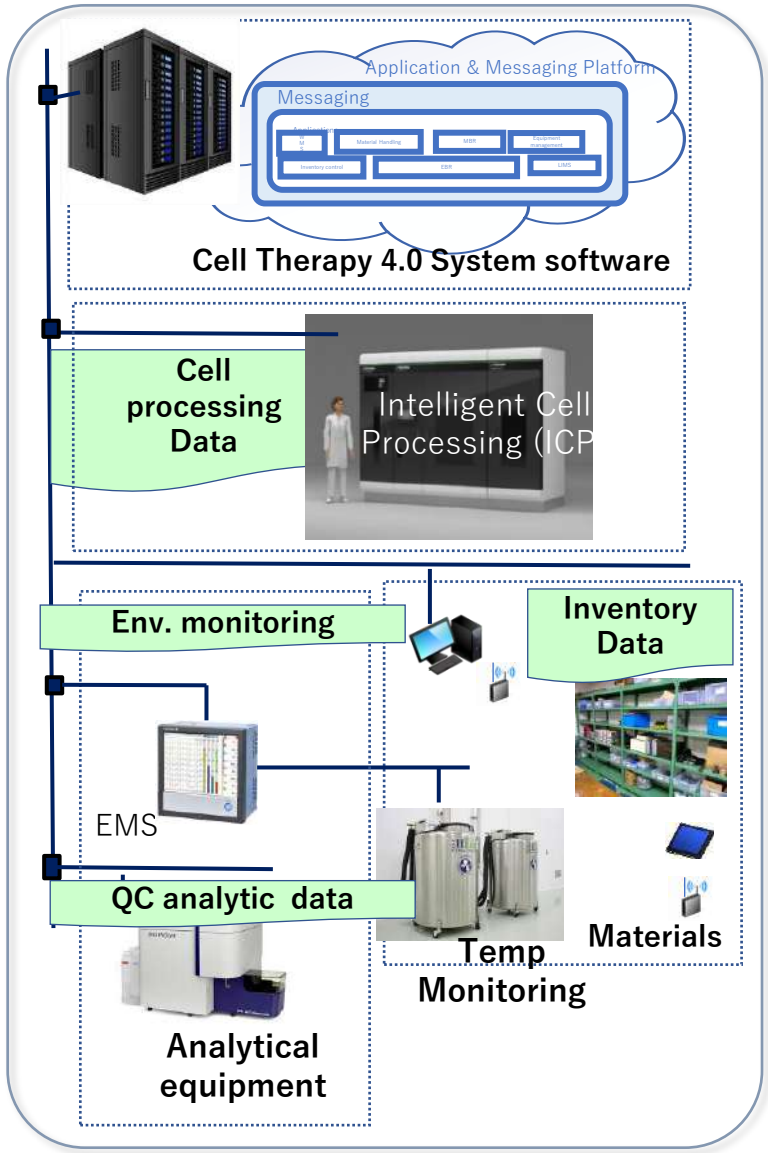
Though digitization of the manufacturing related data.

QbD based-cell manufacturing Solution Lab in KCMI

SINFONIA



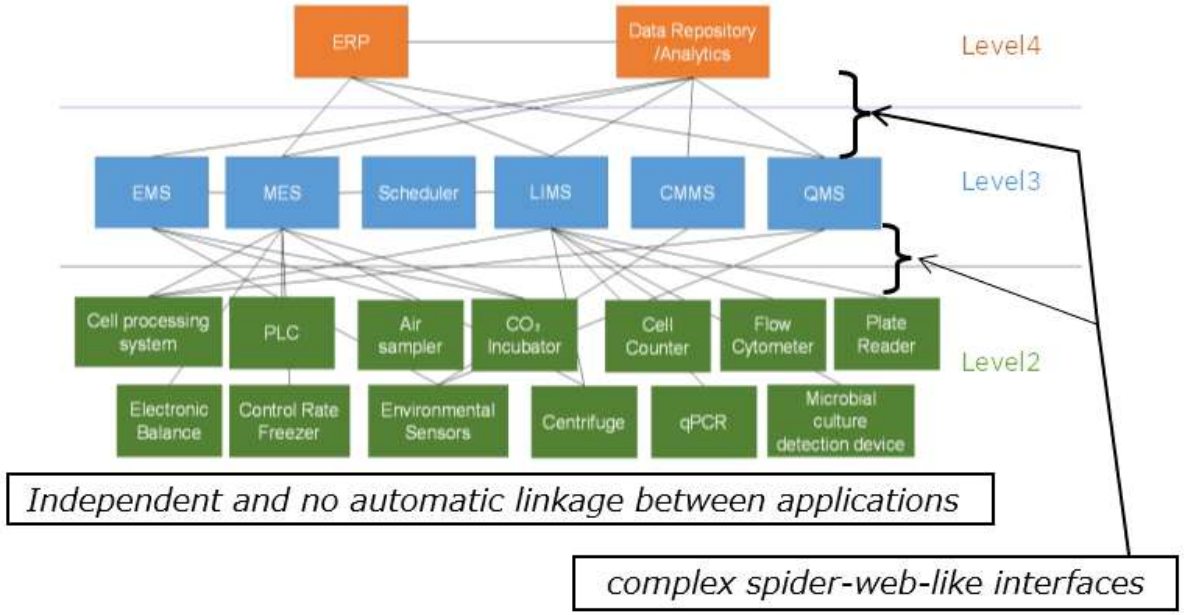
Cloud AMP C&G system



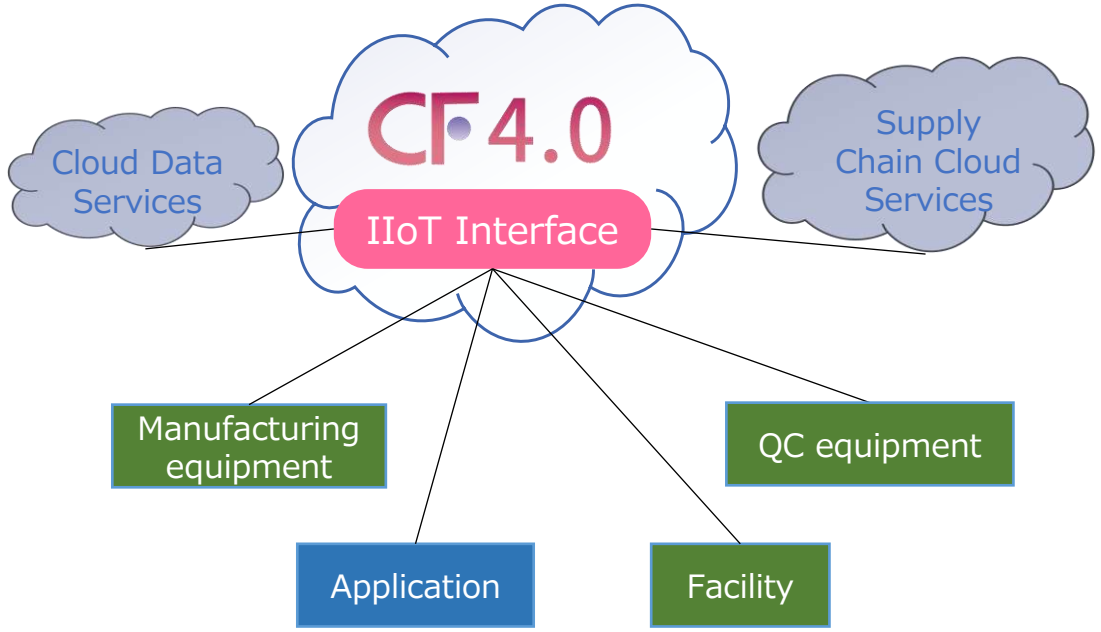
System Architecture

- SaaS Cloud Service (Azure/AWS) connected with secure leased line
- Automatic linkage integrated through IIoT Interface
- Seamless information connection with Manufacturing equipment, QC equipment, Facility, Application, and various Cloud Services

Before

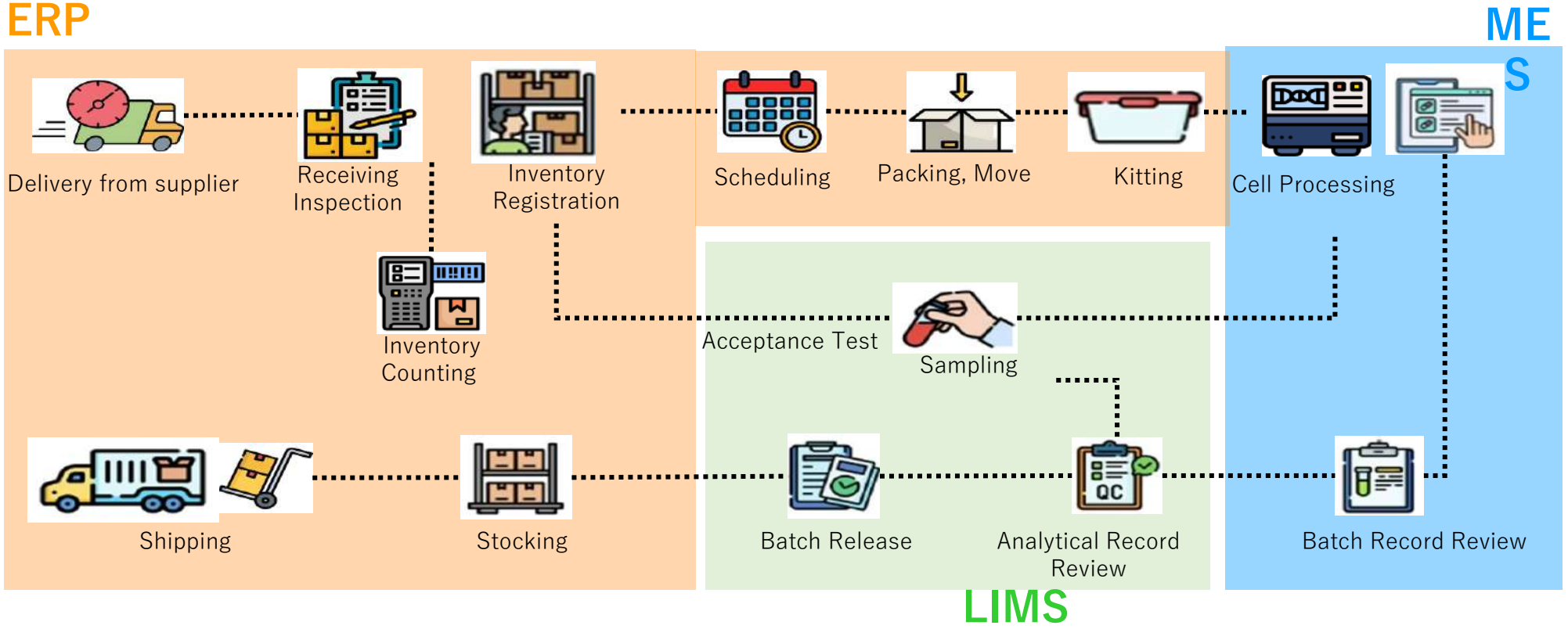


After



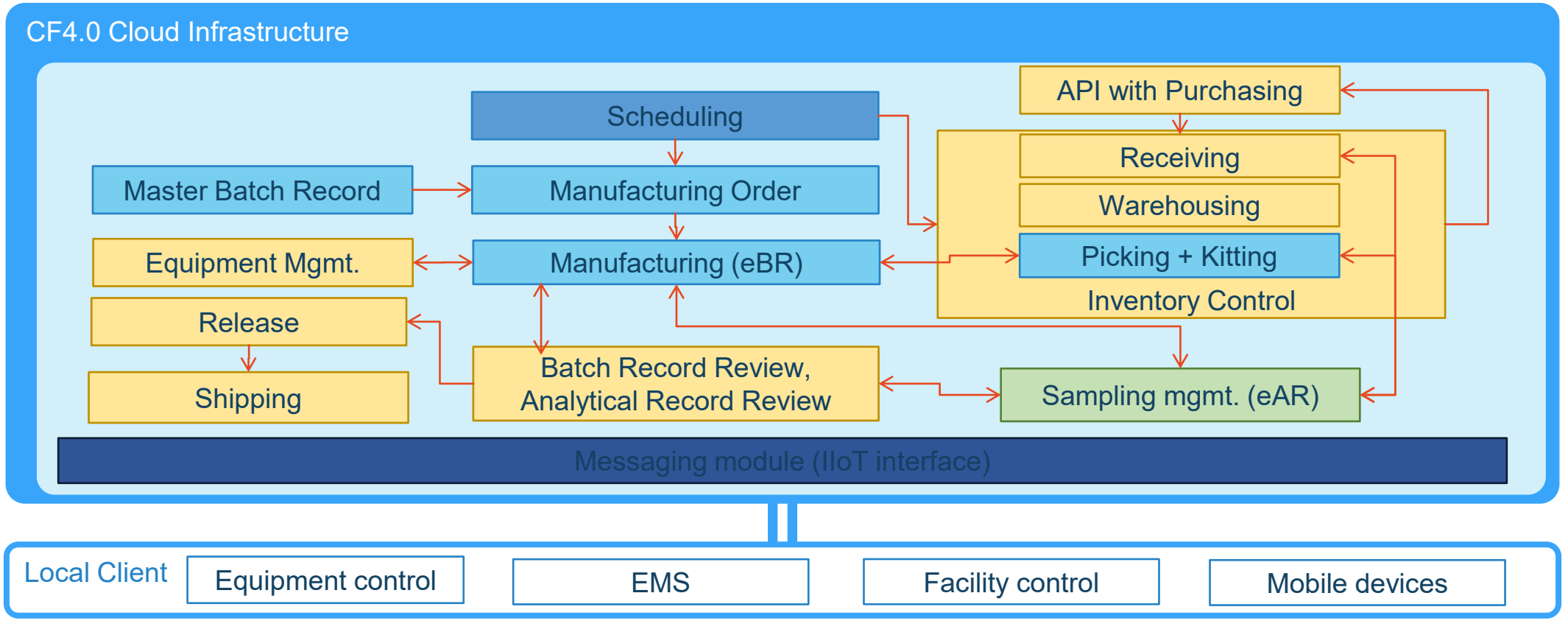
The Conventional System
cannot Fully Manage the Entire Process

- CF4.0 includes all end-to-end standard process models for Cell & Gene Therapy manufacturing in one platform.

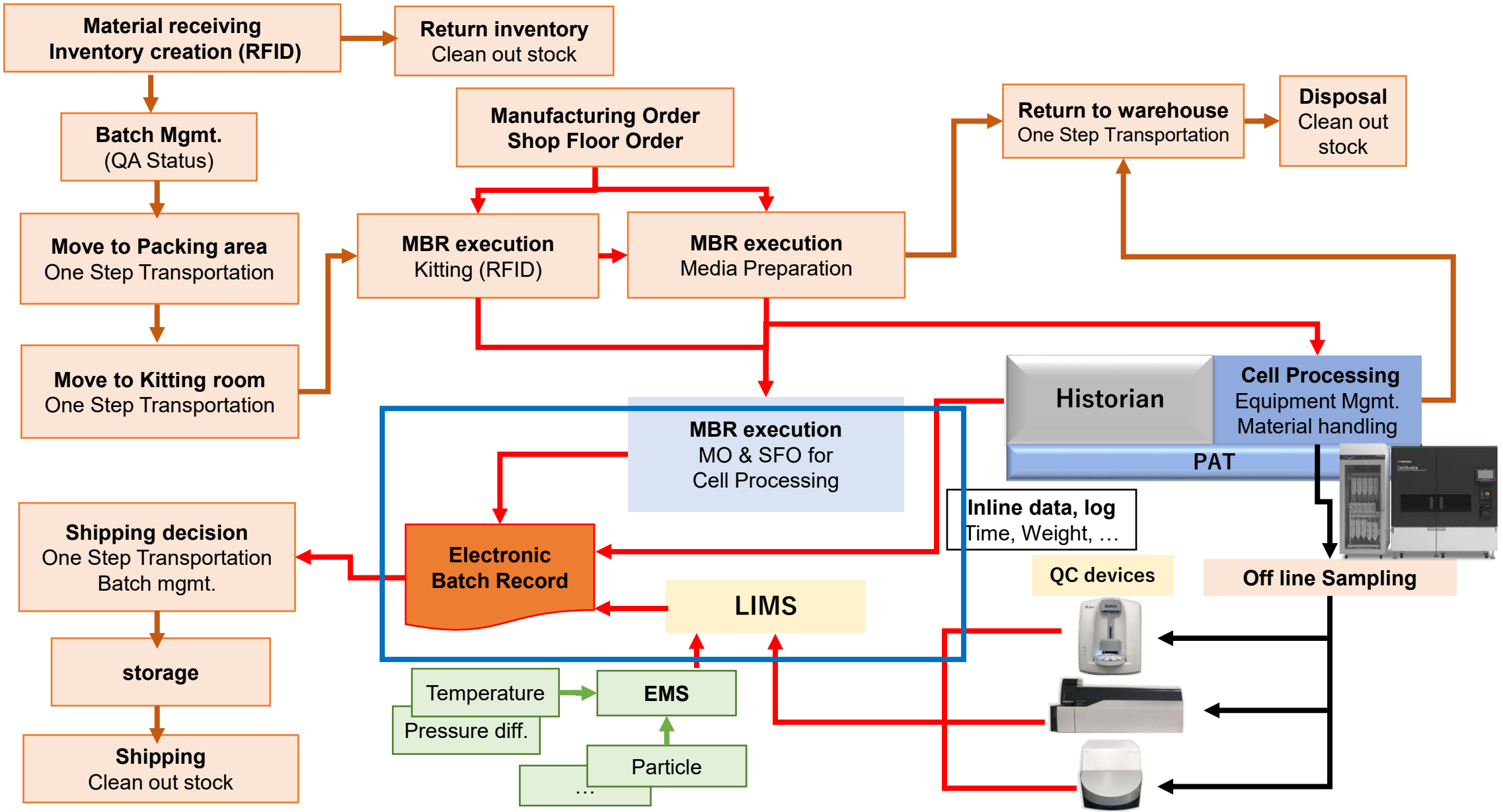


Application Architecture

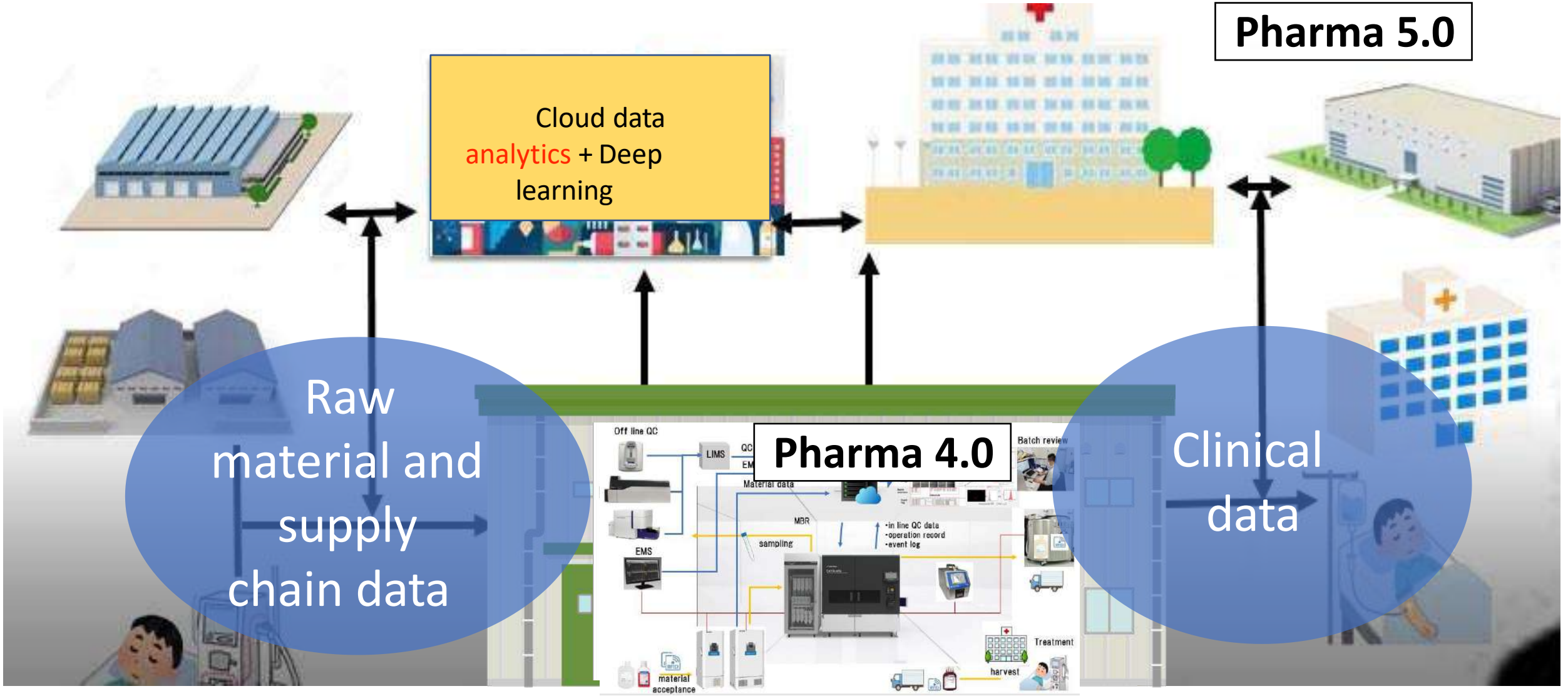
- Provide all necessary functions for Cell & Gene Therapy manufacturing processes
- Integrate all process modules of ERP, MES, LIMS, Scheduling, ⋯ into single on Cloud-based architecture
- Collect all data/records from Equipment, Facility, Mobile, and Application



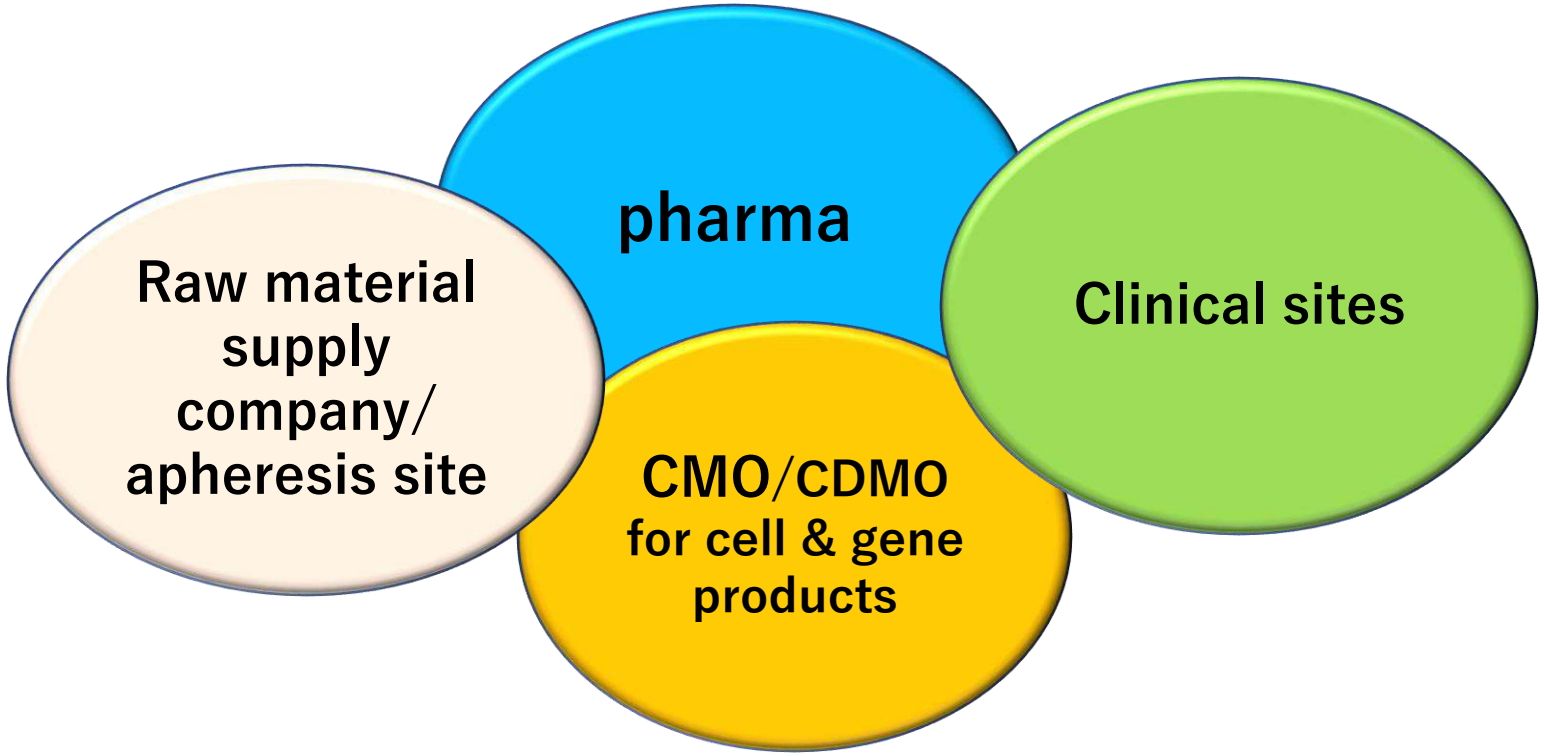
Development of cell manufacturing control system



Manufacturing information in IT format can enable linkage to manufacturing, supply chain and clinical data



For improved treatment outcomes and new drug development, the formation of an ECO system through information sharing is essential.



Manufacturing information shall be digitized on the CMO side to combine it with supply chain and clinical information data

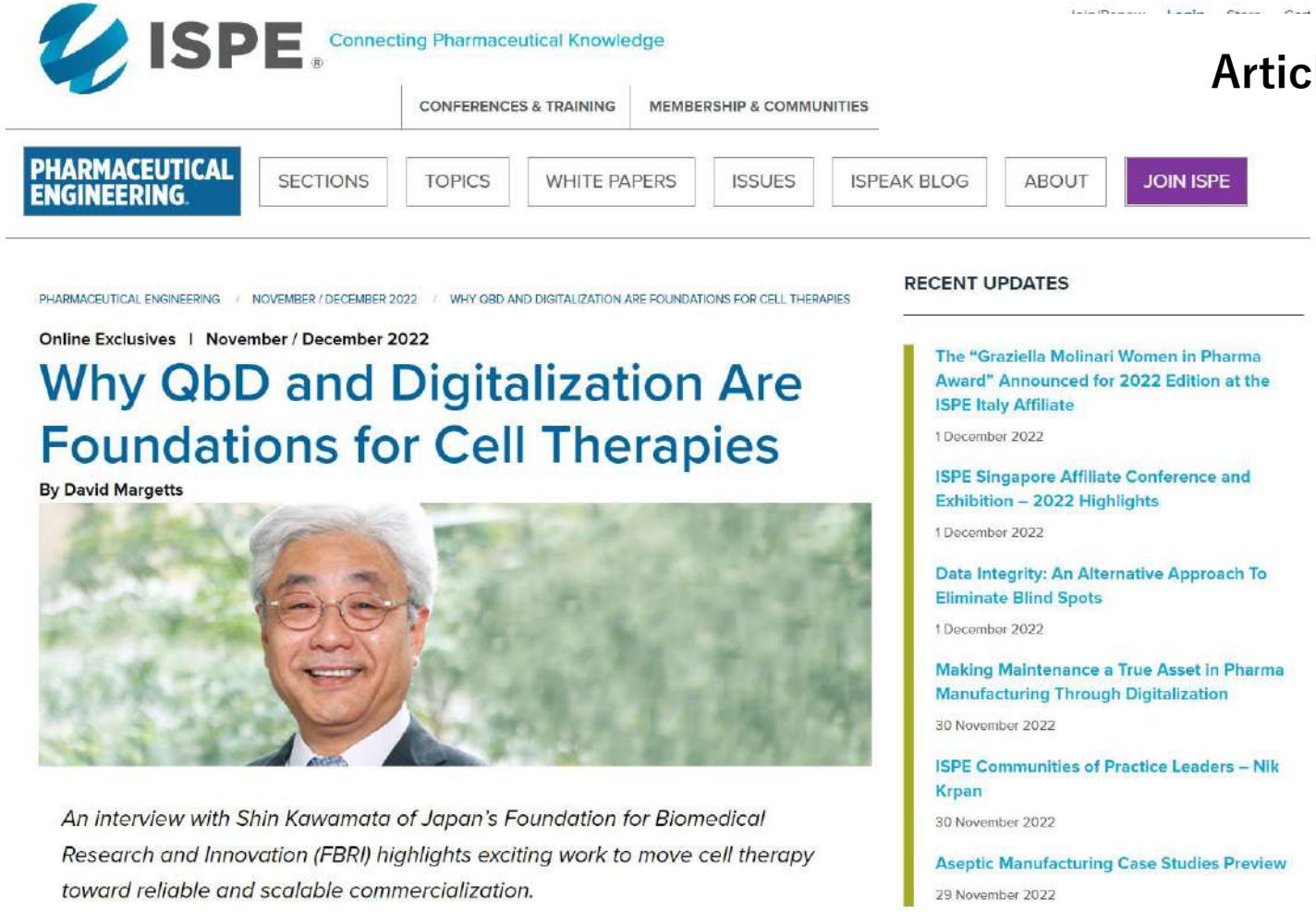
⇒ Need for QbD-based manufacturing

Digitization of process and QC information of cells manufacturing is essential for cell product development

Online Exclusives | November/December 2022

https://ispe.org/pharmaceutical-engineering/november-december-2022/why-qbd-and-digitalization-are-foundations-cell

Article by David Margetts of Factor Talk



ISPE Connecting Pharmaceutical Knowledge

CONFERENCES & TRAINING | MEMBERSHIP & COMMUNITIES

PHARMACEUTICAL ENGINEERING | SECTIONS | TOPICS | WHITE PAPERS | ISSUES | ISPEAK BLOG | ABOUT | JOIN ISPE

PHARMACEUTICAL ENGINEERING / NOVEMBER / DECEMBER 2022 / WHY QBD AND DIGITALIZATION ARE FOUNDATIONS FOR CELL THERAPIES

Online Exclusives | November / December 2022

Why QbD and Digitalization Are Foundations for Cell Therapies

By David Margetts

An interview with Shin Kawamata of Japan's Foundation for Biomedical Research and Innovation (FBRI) highlights exciting work to move cell therapy toward reliable and scalable commercialization.

RECENT UPDATES

The "Graziella Molinari Women in Pharma Award" Announced for 2022 Edition at the ISPE Italy Affiliate
1 December 2022

ISPE Singapore Affiliate Conference and Exhibition – 2022 Highlights
1 December 2022

Data Integrity: An Alternative Approach To Eliminate Blind Spots
1 December 2022

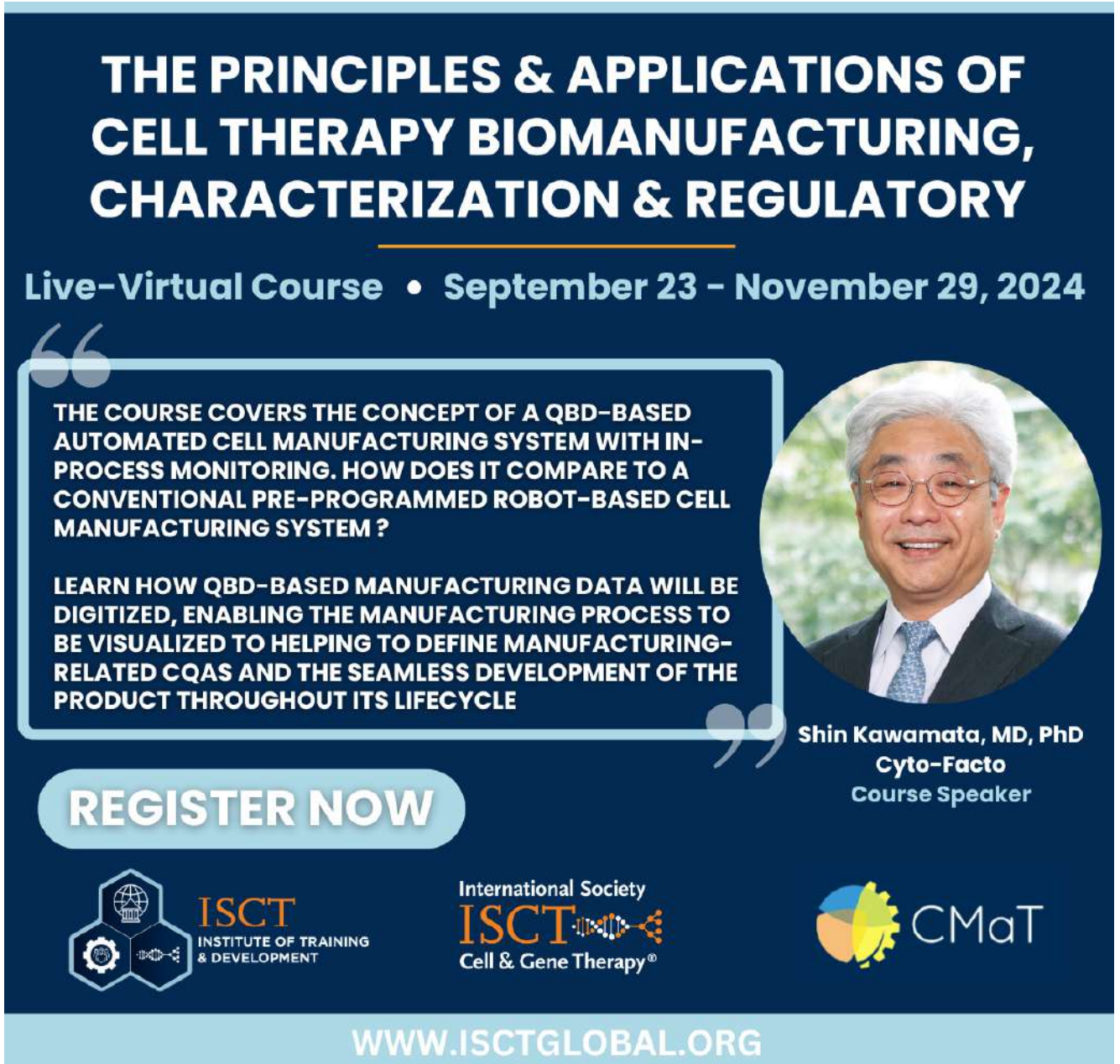
Making Maintenance a True Asset in Pharma Manufacturing Through Digitalization
30 November 2022

ISPE Communities of Practice Leaders – Nik Krpan
30 November 2022

Aseptic Manufacturing Case Studies Preview
29 November 2022

Conducting QbD-based cell manufacturing virtual training course twice/year since 2023

https://drive.google.com/file/d/1XEdlIzMAwkBTwjLAPzS-JPaZyZNeBrZq/view



Support human resource through the ISCT-CMaT training course

- On line lecturing a QbD-based cell manufacturing -

Summary

First, the developer must have an image of the product with defined efficacy and then set up SOPs and process parameters (PPs) within the design space (DS). Next, confirm the quality of the product by ensuring the PPs are within the DS through in-process monitoring. Pharma 4.0 **This is the Quality by Design (QbD)-based manufacturing.**

A robust "efficacy" assay ensures the quality of product manufactured by QbD-based approach. This enables acceptance of changes in raw materials, manufacturing processes, and QC technologies, provided that the product demonstrates the same efficacy.
This is life-cycle development of a product using a QbD-based manufacturing approach.

We can increase new data set leading to the improvement in manufacturing process, selecting new parameters as well as the development of new product, if the digitized manufacturing information obtained by QbD-approach is connected with clinical data.

Pharma 5.0

Thank you for your attention