Establishing an Ethical and Operational Framework for Autologous iPSC-Based Cell Therapy:

A Feasibility Study Using Healthy Volunteers in the "my iPS®" Project

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Toward Responsible Access to Autologous (Patient-specific) iPSCs Produced by an Automated Culture Platform

1 Background

Japan has strict rules for collecting and sharing donor-derived materials. These rules can make autologous (patient-specific) iPSC research more difficult to scale, but they also help build trust. Autologous iPSCs are often discussed in terms of technical challenges: how to generate iPSCs efficiently, how to culture them safely, how to differentiate them into target cells, and how to evaluate their quality. In our foundation, toward the long-term goal of manufacturing transplantable cells tailored to individual patients, we use healthy volunteer-derived cells as a feasibility model to establish automated manufacturing workflows for autologous (patient-specific) iPSCs. Our goal is to establish a trusted system that protects donors while enabling researchers and companies to responsibly access autologous iPSCs generated through automated manufacturing workflows.

A central practical question therefore remains:

How can donor blood be collected and donor-derived iPSCs be shared with other institutions in a way that protects donors and follows national rules?

In Japan, healthy volunteer blood collection cannot simply be expanded through financial incentives. In addition, even de-identified donor-derived iPSCs may require ethical review before being used by recipient institutions. Therefore, access to autologous iPSCs cannot be achieved by a Material Transfer Agreement alone.

2 International Context: Ethical and Regulatory Comparison

The difference between Japan and the United States is not simply whether biospecimens can be transferred. The key difference is how donor protection and identifiability are understood.

United States

Under the U.S. Common Rule, research using coded or de-identified biospecimens may not be considered human subjects research under certain conditions, particularly when investigators cannot readily identify individual donors. Under HIPAA, de-identified health information is generally not subject to restrictions on use or disclosure.

Japan

In Japan, research using human-derived specimens and information is governed by national ethical guidelines for life science and medical research. Blood collection is also conducted within a legal framework emphasizing non-commercial donation and donor protection (e.g., the Blood Act framework).

Even when direct identifiers such as names are removed, genomic analysis may generate information with re-identification potential. Therefore, ethical review and donor protection procedures may still be required when donor-derived iPSCs or associated genomic information are used or shared.

Figure1.Japan vs U.S. governance comparison

	Japan	United States
Recruitment Approach	Volunteer-based recruitment is the norm.(Incentives are generally not permitted)	Incentive-based recruitment(Compensation for time, travel, etc.) is allowed in many cases.
Blood Collection Regulation	Blood collection is regulated under the Act on Securing Safety of Blood Products and Biologics (Blood Act).Strict protection of donors is prioritized.	More flexible biospecimen acquisition models are possible. (Non-clinical research collection is broadly permitted)
Ethics Review After De-identification	Even after de-identification, genomic analysis may generate information with re-identification potential, requiring ethics review in some cases. (Japanese Ethical Guidelines*)	De-identified or coded specimens may not be considered human subjects research under certain conditions (Common Rule).** De-identified information is not subject to HIPAA usage and disclosure restrictions.***
Material Transfer for Research Collaboration	MTA alone may be insufficient; additional ethical/regulatory procedures are often required.	Material transfer via MTA can be conducted more simply in many cases.

- U.S. Common Rule (45 CFR 46) allows certain research using coded or de-identified biospecimens to be excluded from human subjects research oversight under specific conditions.

** Under the HIPAA Privacy Rule (45 CFR 164.514), de-identified health information is generally not subject to HIPAA restrictions

*** In Japan, ethical review requirements may apply to donor-derived specimens and associated genomic information under national ethical guidelines; additional considerations may arise from the legal framework governing blood collection and donor protection.

3 Donor Recruitment and Collection Data

Despite these regulatory and ethical constraints, our donor blood collection activity increased from 8 cases in 2019 to approximately 180 cases per year in recent years.
This does not mean that recruitment is easy. Rather, it shows that a non-commercial, trust-based donor recruitment system can be built step by step.

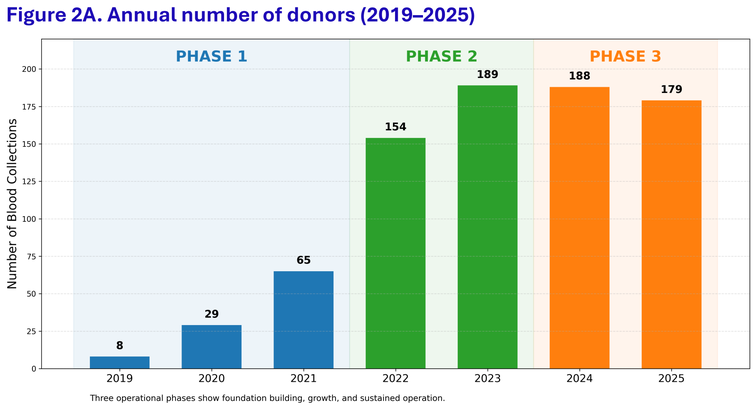
The trend can be understood in three phases:

- **2019–2021: start-up phase (Phase1)**
- **2022–2023: scale-up phase (Phase2)**
- **2024–2025: stable operation phase (Phase3)**

In 2025, monthly blood collection volume also showed that the platform can respond to research demand. This increase may be associated with the growth of collaborative research projects.

Among **25** collaborative research partners, **16** are industry partners, suggesting that there is practical demand from companies developing technologies related to iPSC manufacturing, differentiation, and quality evaluation.

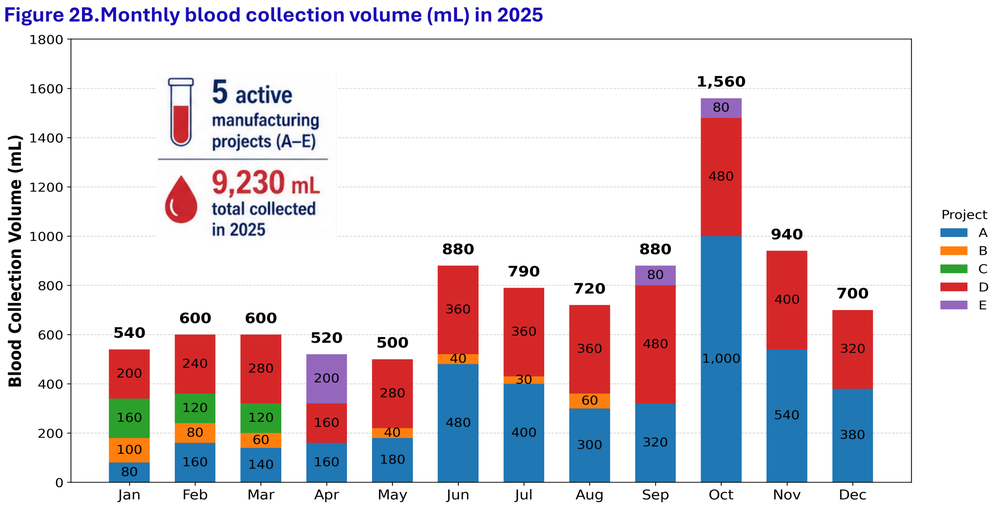
Figure 2A. Annual number of donors (2019–2025)



Total donors (2019–2025)
812 incl. repeats

Even under ethical constraints in Japan, prioritizing donor protection can enable scalable blood collection and support a stable infrastructure for autologous iPSC research.

Figure 2B.Monthly blood collection volume (mL) in 2025



4 Why This Matters for my iPS

For researchers and companies, the main question is not only whether autologous iPSCs can be generated. The practical question is whether they can access well-managed autologous iPSCs for testing technologies.

Our platform can connect three elements:

1. **ethically recruited donor blood**
2. **automated iPSC generation and culture**
3. **collaborative use for differentiation, manufacturing, and quality evaluation studies**

This means that donor-derived autologous iPSCs can become a practical research resource, not only an internal project material.

5 Future Perspective

We aim to make autologous iPSCs generated through automated manufacturing available for responsible collaborative research.
The goal is not simply to distribute cells. The goal is to provide access to cells together with an ethical and operational framework that protects donors and supports reliable use.

Potential collaborative applications include:

- **testing automated culture systems**
- **evaluating differentiation protocols**
- **developing image-based or component-based quality assessment methods**

Key Message

To scale autologous (patient-specific) iPSC research, we need more than manufacturing technology.

We need a trusted system that can collect donor blood ethically, generate iPSCs reproducibly, and allow external researchers to use these resources responsibly.

Conflict of Interest:
The authors declare no conflicts of interest to declare.

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Interested in evaluating automated-manufactured autologous iPSCs for your research?

Let's discuss collaborative applications in differentiation, manufacturing, and quality assessment.

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