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Pluripotent stem cell lines available for use in clinical applications: A comprehensive overview

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SUMMARY

Over the last 25 years, there has been tremendous progress in human pluripotent stem cell (hPSC) technology and clinical trials testing hPSC-derived products. The development of these hPSC-derived products requires the selection of a suitable hPSC line as the starting material for product manufacturing. The bespoke development of an hPSC line for product development can require significant time and resources. Given the acceleration of clinical trials testing hPSC-derived products, there is a growing need for available clinically and commercially suitable "off-the-shelf" hPSC lines. We have identified 166 clinical hPSC lines that are currently available for licensing and distribution. This paper provides details regarding these lines that may assist developers in preliminary evaluation of lines for use in clinical development.

INTRODUCTION

For researchers developing human pluripotent stem cell (hPSC)-derived therapies, selection of the starting material, specifically the hPSC line, to use in clinical manufacture of a drug substance or drug product is one of the most important decisions they will make. It is also one of the biggest pain points they will encounter. Recent reports show that, to date, at least 115 clinical trials using hPSC lines have been performed or are ongoing (Kirkeby et al., 2025). The allogeneic hPSC-derived products in clinical trials have used at least 24 different hPSC lines (Kirkeby et al., 2025). However, the majority of the hPSC cell lines used in the manufacturing of these therapeutics are privately held and are not available for out-licensing. Information on available cell lines is often not readily accessible, and the overall number of available cell lines suitable for clinical development is difficult to assess. Furthermore, information on the lines themselves, and how to obtain and/or license the lines, can be limited or unclear. Therefore, as the number of groups advancing through translational research to clinical application increases, so does the need for readily available good quality, clinically compliant cell lines for use in the development of hPSC-derived therapeutics globally. The ability of researchers to access clinically compliant materials "off-the-shelf' and ready to use rather than deriving bespoke materials can save considerable expense and years of development time.

When choosing an hPSC line, important considerations include the following.

(1) Donor informed consent
(2) Quality systems used to derive and bank the hPSC line, and regulatory compliance
(3) Cell line characterization
(4) Licensing and freedom to operate

This review identifies available hPSC lines that appear to be suitable for use as starting material for hPSC-derived products and provides basic information for review and evaluation to assist hPSC product developers in the selection of starting materials. We have used the aforementioned considerations as a framework and have collected information about these hPSC lines from the published literature and via personal communications with hPSC line manufacturers and distributors. We have identified 166 hPSC lines that are currently available for distribution (Table 1). We hope this information will enable researchers heading toward the clinic to identify and acquire appropriate materials more readily, expediting translation of hPSC research to clinical outcomes.

Informed consent

When selecting an hPSC line for use in the development of therapeutic products, it is important to ensure that the primary donor material was obtained under informed consent. Informed consents will detail how the donor materials will be used, if the donor will be compensated in any way, and the extent to which the donor can control the use of the resulting cell line, among other topics. An example of an informed consent template can be found in the ISSCR guidelines for ethical stem cell research (https://www.isscr.org/guidelines/appendices). As withdrawal of consent following clinical use of a cell line can create significant issues, it is recommended that consent

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Table 1. Available hPSC lines for clinical applications

	Organization information		Number of lines		Quality system	
	Licensing	Distributor	Available for distribution	In clinical trials	Derivation	Banks
hESC lines	Beijing Institute of Stem Cell and Regenerative Medicine	Beijing Institute of Stem Cell and Regenerative Medicine	5	0	research	GMP
	Hadassah Stem Cell Research Center	Hadassah Stem Cell Research Center	7	2	GMP	GMP
	Institute of Zoology, Chinese Academy of Sciences	Institute of Zoology, Chinese Academy of Sciences	1	1	research	research & GMP
	Kyoto University	Kyoto University	10	NR	principles of GMP	principles of GMP
	University of Edinburgh (Roslin Cells)	UK Stem Cell Bank & Scottish National Blood Transfusion Service	3	2	GMP	GMP
	University of Sheffield	United Kingdom Stem Cell Bank	12	0	clean room (HFEA/ HTA License)	clean room (HTA License)
	Wisconsin Alumni Research Foundation (WARF)	WiCell	2	2	research	GMP & research
		TOTAL hESC	**40**	**7**		
hiPSC lines	Allele Biotechnology	Allele Biotechnology	27	0	GMP	GMP
	Catalent Pharma Solutions[a]	Catalent Pharma Solutions	5	0	GMP	GMP
	Cedars Sinai Biomanufacturing Center	Cedars Sinai Biomanufacturing Center	8	0	GMP	GMP & research
	Cellistic	Cellistic	3	0	principles of GMP	GMP
	Center for iPS Cell Research and Application (CiRA)	Center for iPS Cell Research and Application (CiRA)	32	3	GMP	GMP
	ElevateBio	ElevateBio	2	0	principles of GMP	principles of GMP
	Fujifilm Cellular Dynamics (FCDI)	Fujifilm Cellular Dynamics (FCDI)	13	NR	GMP	GMP
	LineaBio	LineaBio	7	0	GMP	GMP
	Lonza/Applied Stem Cell[b]	Applied Stem Cell	3	1	GMP	GMP
		Pluristyx				
	Pluristyx	Pluristyx	10	0	GMP	GMP
	REPROCELL	REPROCELL	16	0	principles of GMP	GMP
		Total hiPSC	**126**	**4**		
Total hPSC			**166**	**11**		

[a]Originally derived by RheinCell.
[b]Originally derived by Lonza. NR, not reported.

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withdrawal be disallowed in jurisdictions where permissible. It is also recommended that nationalistic language is not included in the consent, as it may impact the widespread use of any therapy derived from the materials. It is advisable to ensure that the consent was reviewed by an ethical body that can ensure the rights of the donor(s) are respected. This can be an Institutional Review Board, a Medical Advisory Board, or other appropriate ethical entity charged with representing patient rights. Without this level of ethical review and patient protection, international translation may not be possible.

In some cases, particular topics may not be included in the consent forms given the timing of the donation, or more specifically the status of current technologies at the time of donation and/or derivation. For instance, consents for early human embryonic stem cell (hESC) lines used in clinical trials, such as the University of Wisconsin, Roslin Cells, and Hadassah lines, did not include information about sequencing or gene editing as these technologies were not readily available when the cell lines were derived. However, the absence of specific inclusion within the informed consent does not necessarily preclude the use of these technologies in the development of products from these cell lines. The intent of these informed consents is generally for broad use in research, clinical translation, and commercialization, and risk may be assessed accordingly. Given that these early hESC lines have been successfully used in multiple clinical trials across multiple jurisdictions, the absence of some topics does not preclude the use of these cell lines for translation. Cell lines generated more recently with the specific intent of clinical and/or commercial usage generally include a more comprehensive set of informed consent topics, and it is anticipated that informed consents will continue to evolve as the field progresses.

Quality Systems and regulatory compliance

There are a number of regulatory considerations when evaluating hPSC lines, including Quality Systems used during derivation and banking, reagent quality, and donor eligibility compliance. Regarding Quality Systems, it is important to recognize that initial derivation of a cell line outside of a Good Manufacturing Practice (GMP) Quality System does not, in and of itself, disqualify a cell line from use in clinical and commercial applications. There are a number of hPSC lines that were derived in research labs and have been used to develop products currently being tested in clinical trials (e.g., WA09(H9), WA01(H1), WA07(H7), MA09, I6, and Shef 1) (Kirkeby et al., 2025). These cell lines were some of the earliest hESC lines generated, and although these cell lines were derived under research conditions, subsequent generation of Master Cell Banks (MCB), Working Cell Banks, Drug Substances (DS), and Drug Products (DP) was performed under GMP Quality Systems. In these cases, information about reagents and processes used to derive the cell lines was sufficient to allow risk mitigation strategies and ultimately gain regulatory approval for use in clinical trials.

More recently, hPSC lines for clinical applications have been prospectively generated under GMP-compliant conditions (Baghbaderani et al., 2015; Crook et al., 2007; De Sousa et al., 2016; Tannenbaum et al., 2012; Yoshida et al., 2023). In these cases, reagent quality and safety testing have been performed under GMP Quality Systems. For the generation of hESCs under GMPs, the In Vitro Fertilization (IVF) IVF process used to generate the blastocyst starting material is generally not a GMP process, but downstream activities are performed under GMP. In addition to these GMP-derived lines, several manufacturers have developed hPSC lines under the "Principles of GMP." This typically involves using fit-for-purpose reagents, documentation, traceability, and assays, coupled with risk mitigation strategies to ensure safety. Often, this amounts to using GMP systems but not performing the cell line derivation in a GMP suite.

When considering regulatory compliance, it is important to recognize that specific requirements vary across jurisdictions. Adherence to donor eligibility requirements requires careful evaluation. In most jurisdictions, regulatory authorities require donor testing and screening, meaning that the donor of the tissues (e.g., blastocysts, blood, and fibroblasts) used to generate the hPSC line should undergo specific tests for pathogens and infectious agents and answer questions regarding medical, travel, and/or lifestyle information. In most jurisdictions, the timing of donor screening and testing is within days or weeks of tissue harvest. It is of note that this timing is not compatible with the logistics of hESC derivation. In most cases, the donation of embryos for hESC line derivation is separated in time from the generation of the embryos, sometimes by many years. Therefore, compliance with the timing requirements for donor screening and testing is not possible. However, risk mitigation strategies, including but not exclusive to adventitious agent testing of the MCB, have been utilized to permit the use of these cell lines in clinical applications.

Reagent use in all stages of manufacturing can impact translation and is important to carefully evaluate. Exposure to prions (e.g., bovine spongiform encephalopathy and Creutzfeldt-Jakob disease) can cause significant concern in some jurisdictions. Because there is currently no validated test for prion detection available, the use of cell lines generated from UK or European donors, or biological reagents sourced from these areas, can be problematic for use within the US. Additionally, the use of xenogeneic reagents during hPSC manufacturing can result in differing regulatory approval processes and possibly the need for

additional safety testing to meet requirements depending on the region. For instance, in some cases, hESCs have been derived and expanded on murine feeders. Under Food and Drug Administration (FDA) regulatory guidance, the co-cultivation of human cells with other species renders the resulting product xenogeneic, which is subject to the guideline for xenogeneic products (Center for Biologics Evaluation and Research, 2016). However, EU guidelines do not categorize these types of products as xenogeneic products (EMEA, 2009). Therefore, when assessing materials, it is important to consider the regions in which the final product will be used, and care should be taken to carefully evaluate materials to ensure compliance with use in the desired region(s). Deficiencies in certain areas, however, may not inhibit the ability to use the materials in clinical applications. If there are concerns, development of risk mitigation strategies and early consultation with regulators is advisable.

A number of hPSC line manufacturers have filed a Drug Master File (DMF) with the US FDA, an Active Substance Master File in the EU, or a Master File with the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan. These documents contain Chemistry, Manufacturing, and Controls information used to develop and characterize the hPSC line. This can facilitate the application process for Sponsors as they file their Investigational New Drug (IND) and/or Clinical Trial Application. In some cases, hPSC line developers may have proprietary manufacturing processes that they do not wish to share with the Sponsor. The filing of these documents with regulatory authorities allows this confidential information to be reviewed by those authorities without being disclosed to the Sponsor. In the US, the manufacturer can provide a Letter of Access (LOA) to the Sponsor, which allows FDA reviewers to access the DMF. It is important to note that filing a DMF with FDA does not mean that FDA approves the cell line; the DMF is not reviewed by FDA until a Sponsor files an IND or other regulatory document with an LOA to the DMF.

Cell line characterization

The ability of a cell line to differentiate properly and maintain genomic integrity is essential for the assurance of manufacturing performance and consistent production of DS/DP. This makes the evaluation of the ability to differentiate and of genomic integrity critical in the selection of candidate cell lines for therapeutic use. The ability to differentiate into three germ layers is a defining feature of a pluripotent stem cell (PSC). Pluripotency can only be definitively demonstrated through differentiation into cell types representing endoderm, mesoderm, and ectoderm. Previously, teratoma formation in immunocompromised animals was considered the standard for demonstrating pluripotency. However, more recently, studies have shown *in vitro* differentiation and assessment of gene expression to be adequate and appropriate for determining pluripotency (International Stem Cell Initiative, 2018), and cell line developers and/or manufacturers generally use these methods to demonstrate this potential as part of a cell characterization program. However, this does not ensure efficient differentiation to specific cell types, and additional analysis may be desired to confirm suitability of the cell line for the intended use.

It is well known that PSCs can accumulate genetic mutations in culture (Draper et al., 2004; International Stem Cell Initiative et al., 2011; Mayshar et al., 2010; Weissbein et al., 2014). Mutations that occur most frequently, termed "recurrent abnormalities" in PSCs, include changes in chromosomes 1, 12, 17, 18, 20, and X (Baker et al., 2016; Draper et al., 2004). These changes can impact the structure and function of the pluripotent cells and their differentiated lineages and should be avoided. In the last decade, sensitive tools to assess genetic mutations have become more readily available. As such, assessment of the genome is recommended. While there are many different methods that can be appropriately used to assess the genome of the cell line (Standards for Human Stem Cell use in Research, 2023), karyotyping by g-band is common practice for high-level routine monitoring, and whole-genome sequencing or exome sequencing of hPSC lines has become quite common. In addition, regulatory agencies have begun recommending sequencing of cell lines that have been in extended culture and/or that have been edited (Center for Biologics Evaluation and Research, 2024). Several of the hPSC manufacturers have sequenced the available cell lines, and some have assessed these data using oncogene panels. While it is generally recommended to avoid cell lines that have TP53 mutations (Center for Biologics Evaluation and Research, 2024), it is more complex to determine if mutations in other oncogenes present risks to patients; this is often dependent upon the patient population and the product risk profile.

There are other hPSC qualities that may influence the selection of an hPSC line, such as blood type, human leukocyte antigen (HLA) expression, and/or adventitious agent testing. Several hiPSC providers have selected donors based on blood type and HLA, preferring type O donors with homozygous HLA alleles. This preference is based on the assumption that a DP generated from a type O cell line may be less immuno-reactive upon implantation into a patient. The same argument has been put forward for HLA homozygosity, especially when the donors have been selected to represent the most common HLAs in a particular region. For example, Center for iPS Cell Research and Application (CiRA) generated 27 human induced pluripotent stem cell (hiPSC) lines using donors selected for homozygosity on the most common Japanese HLAs to create a haplobank

matching approximately 40% of the Japanese population (Yoshida et al., 2023).

Lines may also be chosen based on sex. Some groups prefer female cell lines due to concerns about possible increased immunogenicity in female recipients caused by expression of minor histocompatibility antigens encoded on the Y chromosome (Hu et al., 2020). In contrast, some groups prefer male cell lines due to concerns about erosion of X inactivation, which may represent genetic or epigenetic instability (Bar and Benvenisty, 2019; Bar et al., 2019). Adventitious agent testing may also be a critical factor, as apart from the obvious, it may impact the ability of a cell line to be accepted into a manufacturing facility for further development. Knowledge regarding which specific tests are required in your region of interest is advised.

Freedom to operate and material rights

A clear understanding of the Intellectual Property (IP) and material rights associated with the cell line of choice is important, and it is advisable to perform sufficient due diligence to ensure a clear line of sight to licensing critical technologies prior to the initiation of a translational program. Resolving issues early is highly advisable, as failure to do so may result in a necessary change in material(s) and/or reagents later in product development that can result in increased time and cost. Product goals may influence the evaluation and ultimate cell line selection. If the goal is to develop a commercialized product, the IP and licensing will be more critical. In this review, we provide information about providers (owners) and/or distributors who can be contacted to gather information about freedom to operate (FTO) and licensing considerations (Tables 1, S1, and S2). While this information should be helpful, it is not intended to be all inclusive, and each Sponsor will need to perform due diligence on the individual lines for use in their desired indication.

Both IP and material rights can be associated with any of the technologies or reagents used in hPSC line manufacturing. It is important to assess all aspects critical to the development process including but not limited to reprogramming technology, vectors, reporters, delivery method of reprogramming factors, materials and reagents, and any product that comes into contact with the cells or enters the manufacturing pipeline and to determine if licensing is required and if it can be obtained. Also, be aware that patents are not issued globally but rather are filed nationally. Therefore, when planning clinical trial or commercialization locations, one may want to consider the jurisdictional requirements for licensing and FTO. The time limitations for patents may also be contemplated. For instance, in the US, patent rights are held for about 20 years after which licensing may no longer be required.

In contrast, material rights persist indefinitely, and cell lines are licensed from the owner/provider independent of IP status. Material rights may be required for investigative research, translational, clinical, therapeutic, and/or commercial use, and it is recommended to be obtained prior to use of the materials. This is usually done via a material transfer agreement, label license, or a similar document that outlines restrictions on use of the cell line and should be carefully reviewed to ensure compliance.

RESULTS AND DISCUSSION

We have identified 166 hPSC lines apparently suitable for clinical applications that are currently available from 18 independent distributors (Table 1). Of these 166 PSC lines, 40 are hESC lines and 126 are iPSC lines. Of note, nearly 50% (59 lines) of the available iPSC lines are held by 2 providers. In addition to the hPSC lines that are currently available for distribution, we identified another 45 hPSC lines that were generated with the intention of use in clinical applications but are either not currently available (due to the lack of an existing distribution lot or potential licensing restrictions) or we have been unable to confirm the information and accessibility of the lines (Table S3). It is possible that these lines may become available in the future, and licensing organization information has been provided to enable further inquiry (Tables S1 and S2).

Clinical trials to date

The first clinical trial using hPSCs was initiated in 2010 (Figure 1A) (Kirkeby et al., 2025). Since that time, clinical trials have been initiated every year, with the number of trial initiations peaking in 2020, 10 years after the initial trial was launched. Cumulatively (Figure 1B), the number of clinical trials testing hPSC-derived products has increased steadily over the last 15 years (Figure 1B). From 2010 through 2019, clinical applications of hPSC technology favored hESC lines (Figure 1A); however, the discovery of the first human hiPSCs in 2007 (Takahashi et al., 2007; Yu et al., 2007) was 9 years behind the development of hESCs, and the similarly timed lag in uptake is likely simply due to accessibility of materials as research on many hESC-derived products would have been initiated before the discovery of hiPSCs. More recently, the use of hiPSCs to develop clinical products has risen to be relatively similar to that of hESC (Figure 1B). While more recently the use of hiPSCs has outpaced the use of hESCs in the development of clinical products, the number of trials testing either hESC products or hiPSC products remains similar, and products developed from hESCs continue to make up a significant portion of trials initiated. Of the available hPSC lines identified, products using 7 hESCs and 4 hiPSC

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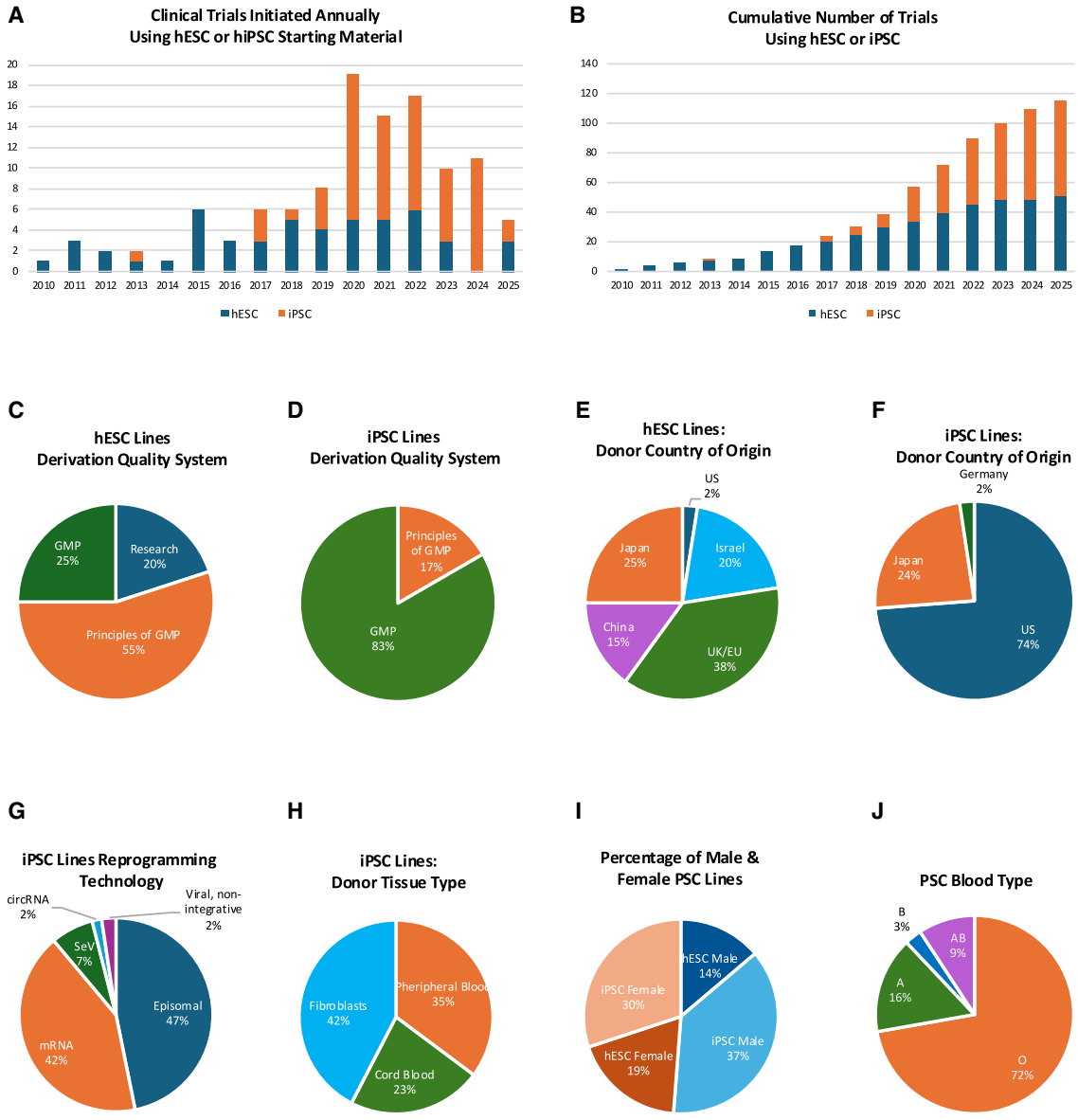

Figure 1. hPSC lines for clinical applications

Percentages reported are rounded to the nearest whole number.

(A) Clinical trials initiated annually using hPSC starting material.

(B) Cumulative number of clinical trials using hPSCs over time.

(C) Percentage of available hPSC lines derived using different quality systems.

(D) Percentage of available hiPSC lines derived using different quality systems.

(E) Donor country of origin for available clinical hPSC lines.

(F) Donor county of origin for available clinical hiPSC lines.

(G) Reprogramming technologies used for the generation available of hiPSCs.

(H) Donor tissue type used as starting material for available hiPSC line generation.

(I) Percentage of male and female available hPSC lines.

(J) Blood type of available hPSC lines.

Table 2. Available clinical hPSC lines currently in clinical trials

Distributor	Cell line	Product name	Source	Indication	Sponsor	Jurisdiction	Trial ID	Study phase
Center for iPS Cell Research and Application (CiRA)	QHJI01s04	iPSC-RPE cell suspension	hiPSC	neovascular AMD	Kobe City Eye Hospital	JP	UMIN000026003	1
		aiPSC-RPE CSt	hiPSC	RPE impaired disease	VCCT	JP	jRCTa050210178	1/2
		Retinal organoid sheets	hiPSC	retinitis pigmentosa	CiRA	JP	jRCTa050200027	1
		CLS001	hiPSC	bullous keratopathy	Keio University	JP	jRCTa031210199	1
		iPSC-derived DA progenitors	hiPSC	PD	Kyoto University Hospital	JP	UMIN000033564	1/2
		CM patch	hiPSC	ischemic heart disease	Osaka University	JP	NCT04696328	1
			hiPSC	heart failure	CiRA, Osaka University	JP	jRCT2053190081	1
		ICAR-ILC/N101	hiPSC	ovarian clear cell carcinoma	CiRA, National Cancer Center Hospital East, Harano Kenichi	JP	jRCT2033200431	1/2
	YZWJs524	iCEPS	hiPSC	limbal stem cell deficiency	Osaka University	JP	UMIN000036539	1
	YZWJs513	hiPSC-NS-PCs	hiPSC	SCI (th, cer)	Keio University	JP	UMIN000035074	1/2
		MEG-002	hiPSC	thrombocytopenia	Megakaryon Corp.	JP	JRCT2053210068	1/2
Chinese Academy of Sciences	CH1 (Q-CTS-hESC-2)	hESC-RPE	hESC	wet AMD, SMD	Southwest Hospital	CN	NCT02749734	1/2
		hESC-RPE	hESC	dry AMD	Chinese Academy of Sciences	CN	NCT02755428	1/2
		DA progenitors	hESC	Parkinson's disease	Chinese Academy of Sciences	CN	NCT03119636	1/2
		MSC	hESC	primary ovarian insufficiency	Chinese Academy of Sciences	CN	NCT03877471	1
		MSC	hESC	intrauterine adhesions	Chinese Academy of Sciences	CN	NCT04232592	1
		MSC	hESC	COVID-19	Chinese Academy of Sciences	CN	NCT04331613	1/2
		MSC	hESC	pulmonary fibrosis from COVID-19	Wuhan Jinyintan Hospital	CN	ChiCTR2000031139	1
Hadassah Stem Cell Research Center	HAD-C 102	RG6501 (OpRegen)	hESC	advanced dry-form AMD	Hoffman-La Roche	US, IL	NCT02286089	1/2
			hESC	AMD	Genentech	US, IL	NCT05626114	2
	HAD-C 100	AstroRx	hESC	ALS	Kadimastem	IL	NCT03482050	1/2
Pluristyx	LiPSC-GR1.1 (TC1133)	MyoPAXon	hiPSC	Duchenne muscular dystrophy	University of Minnesota	US	NCT06692426	1
		EHM	hiPSC	advanced heart failure	University Medical Center of Göttingen	DE	NCT04396899	1/2

(*Continued on next page*)

Table 2. *Continued*

Distributor	Cell line	Product name	Source	Indication	Sponsor	Jurisdiction	Trial ID	Study phase
UK Stem Cell Bank & Scottish National Blood Transfusion Service	RC-9	Patch ISTEM-01	hESC	retinitis pigmentosa due to monogenic mutation	iSTEM	FR	NCT03963154	1/2
	RC17	STEM-PD	hESC	PD	Region Skåne	SE, UK	NCT05635409	1/2
WiCell	WA01(H1)	GRN-OPC1	hESC	SCI (th)	Geron Corp & Lineage Cell Therapeutics	US	NCT01217008	1
		AST-OPC1	hESC	SCI (cer)	Lineage Therapeutics	US	NCT02302157	1/2
		AST-VAC2	hESC	non-small cell lung cancer	Cancer Research UK	UK	NCT03371485	1
	WA09(H9)	CPCB-RPE1	hESC	AMD	Regenerative Patch Technologies	US	NCT02590692	1/2
						US	NCT06557460	2
		hESC RPE	hESC	wet/dry AMD, SMD	Federal University of Sao Paulo	BR	NCT02903576	1/2
		Bemdaneprocel	hESC	PD	BlueRock Therapeutics	US, CA	NCT04802733	1 & 3
		NR1-02	hESC	stroke	Stanford University	US	NCT04631406	1/2

US, United States of America; JP, Japan; FR, France; DE, Germany; IL, Israel; SE, Sweden; CN, China; Brazil, BR.

lines are currently being tested in 20 and 13 clinical trials, respectively (Table 2). These numbers are likely low, as they only reflect publicly available information; some Sponsors have not disclosed which cell line(s) they are using as their starting material. In addition, many of the trials testing hiPSC-derived products use bespoke hiPSC lines that are not currently available for distribution.

Informed consent

Donor informed consent was obtained for all of the 166 available hPSC lines identified (Table 3). All of the informed consents included consent for hPSC line generation, use of the cell lines for commercialization, and assurances that donor information will remain anonymized. Consents for the hESC lines did not include that the cell line may be genetically modified or that analysis of the genetic data may allow identification of the donor. This is not surprising, as the majority of the clinically compliant hESC lines currently available were derived before sequencing and genomic editing technologies existed or were widely available.

Donor information

The country of origin of the donors that provided the starting tissue for hPSC generation is of interest as it impacts regulatory compliance, as mentioned earlier. For the 40 available hESC lines, 38% of the embryos are from the UK, 25% from Japan, 20% from Israel, 15% from China, and 2% from US (Figure 1E). Clinical trials have been initiated using materials from most of the regions represented. Of the identified 126 hiPSC lines, 74% were from US donors, 24% from Japan, and 2% from Germany (Figure 1F). The donor tissues used to generate the hiPSC lines are split fairly equally between fibroblasts, peripheral blood, and cord blood (Figure 1H).

Donor HLA and blood type may also be considerations in selecting a cell line. The prospective generation of hPSC lines for clinical applications has allowed the inclusion of HLA and blood type for donor selection. Several manufacturers, such as CiRA, Fujifilm Cellular Dynamics, and others, have specifically selected donors that are homozygous for the most common HLAs in the target jurisdiction (Baghbaderani et al., 2015). Of note is that, of the 166 hPSC lines available, at least 78 of these have been reported to be type O blood type (Figure 1J).

A number of groups deriving hPSC lines for clinical applications have worked to include donors that broadly cover a diverse population. This is done by selecting HLAs that are common to different demographics as well as selecting donors with blood type O. It is interesting to note that for hESC lines, 1 line is generated from 1 donor, while for hiPSCs, 1 donor usually gives rise to multiple lines. In the analysis presented here, 40 hESC lines were generated from 40 embryos while the 126 hiPSC lines were derived from 51 US, Japanese, and German donors (Table 1; Figures 1E and 1F; Table S2). The sex of the PSC line can

Table 3. Informed consent information for available clinical hPSC lines: Information included

	Licensor/distributor																	
	hESC lines							hiPSC lines										
Included in donor informed consent	Beijing Institute of Stem Cell and Regenerative Medicine	Hadassah Stem Cell Research Center	Institute of Zoology, Chinese Academy of Sciences	Kyoto University	University of Edinburgh (Roslin Cells)/ Scottish National Blood Transfusion Service	University of Sheffield/ UK Stem Cell Bank	Wisconsin Alumni Research Foundation (WARF)/ WiCell	Allele Biotechnology	Catalent Pharma Solutions	Cedars Sinai Biomanufacturing Center (CBC)	Cellistic	Center for iPS Cell Research and Application (CiRA)	ElevateBio	Fujifilm Cellular Dynamics (FCDI)	LineaBio	Lonza; Applied Stem Cell/ Pluristyx; Applied Stem Cell	Pluristyx	REPROCELL
Consent from both donors	+	+	+	+	+	+	+	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Consent for PSC generation	+	+	+	+	+	+[a]	+	+	+	+	+	+	+	+	+	+	+	+
Human transplantation	+	+	+	+	+	+	+	+	+	+	+	+	NR	+	+	+	+	+
Commercialization	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cannot withdraw consent following derivation of cell line	-	-	-	+	+	+	[b]	+	+	+	+	+	NR	+	+	+	+	+
Cannot direct use of cell line	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+
Donor info will remain anonymized	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Analysis of genetic data may allow identification of donor	-	-	-	-	-	-	-	+	*	-	+	+	+	+	-	-	+	-
Cell line may be genetically modified	-	-	-	-	-	-	-	+	+	+	+	+	NR	+	+	+	+	+
Donor will not be compensated	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+

+ included in consent form.
- not included in consent form.
NR, not reported.
N/A, not applicable.
[a]Included in patient information sheet.
[b]Dependent on line, confirm with distributor.

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Table 4. hESC line quality systems, regulatory compliance, and available banks for currently available hESC lines

Licensor/distributor		Beijing Institute of Stem Cell and Regenerative Medicine	Hadassah Stem Cell Research Center	Institute of Zoology, Chinese Academy of Sciences	Kyoto University	University of Edinburgh (Roslin Cells)/ Scottish National Blood Transfusion	University of Sheffield/UK Stem Cell Bank	Wisconsin Alumni Research Foundation (WARF)/WiCell
Regulatory filings	Drug Master File (or similar)	no	no	no	NR	NR	NR	DMF with FDA FMF with FDA
Donor screening & testing	donor screening & history	yes	yes	yes	yes	yes	no	no[a]
	donor testing	yes	yes	yes	yes	yes	yes	no[a]
	timing of donor screening & testing	N/A	prior to gamete retrieval & >5 years after embryo generation	N/A	NR	NR	prior to embryo generation	N/A
Derivation information	embryo country of origin	China	Israel	China	Japan	UK	UK	USA or Israel
	date of gamete retrieval – before or after May 25, 2005	after	before	after	after	after	before	before
	quality system	research	GMP	research	principles of GMP	GMP	research	research
	use of feeders – human or mouse	human	human	human	no	human	dependent on line	mouse
	use of xeno reagents	no	no	no	no	yes	yes	yes
	use of human reagents	yes	yes	yes	NR	yes	dependent on line	yes
	complete reagent list available – catalog numbers and lot numbers	yes	yes	yes	data available	yes	dependent on line	catalog numbers & some lot numbers
	production records available	yes	NR	yes	data available	yes	yes	yes

(*Continued on next page*)

Table 4. *Continued*

Licensor/distributor		Beijing Institute of Stem Cell and Regenerative Medicine	Hadassah Stem Cell Research Center	Institute of Zoology, Chinese Academy of Sciences	Kyoto University	University of Edinburgh (Roslin Cells)/ Scottish National Blood Transfusion	University of Sheffield/UK Stem Cell Bank	Wisconsin Alumni Research Foundation (WARF)/WiCell
Banks available for distribution	quality system	GMP	GMP	research & GMP	principles of GMP	GMP	HTA licensed Clean Room	research & GMP
	use of feeders	no	human	no	no	no	dependent on line	no
	use of xeno reagents	no	no	no	no	no	dependent on line	yes
	passage numbers of available banks	P16–P28	P11–P26	P33	data available	NR	P5–P17	P28 & P29

NR, not reported.
N/A, not applicable.
Additional information on unavailable lines can be found in Table S1.
[a]Tissues collected prior to May 25, 2005 are not required to comply with 21 CFR 1271 Donor Eligibility Regulations.

also influence cell line selection. Overall, the proportion of male and female lines is similar; 51% of the lines are male, and 49% are female (Figure 1I).

Quality Systems used

Evaluation of the Quality Systems used to derive hPSC lines showed that the majority of both hESC and hiPSC lines were derived under GMPs or principles of GMP (Tables 4 and 5). Of the 40 available hESC lines, 20% were derived in research conditions, 55% were derived under the principles of GMP, and 25% were derived under GMPs (Table 1; Figure 1C). Of the 7 hESCs that are currently being tested in clinical trials, 3 were derived under research conditions (WA09, WA01, and CH1 [Q-CTS-hESC-2]), and 4 were derived under GMPs (HAD-C 100, HAD-C 102, RC-9, and RC-17) (Table 2).

Of the 126 available hiPSC lines, 17% were derived under the principles of GMP and 83% were derived under GMPs (Table 1; Figure 1D). In contrast to hESC derivation, it is interesting to note that the 4 hiPSC lines we have identified as being tested in clinical trials were all derived under GMPs by either CiRA (Yoshida et al., 2023) or Lonza (Baghbaderani et al., 2015). Although these lines were derived under GMPs, some unedited and edited hiPSC lines in clinical trials that are not currently available for distribution were generated under the principles of GMP, indicating that GMP hiPSC derivation may not be essential in some jurisdictions.

Reprogramming technologies used

As mentioned previously, when selecting an hiPSC line, it can be important to consider the reprogramming technology used to generate the line. The IP landscape for reprogramming technologies can be quite complex and it is important to ensure that appropriate technology licenses can be secured. The different groups generating, banking, and distributing hiPSC lines have used different reprogramming technologies, some of which are proprietary to the manufacturer/distributor. Of interest, the majority of the hiPSC lines were reprogrammed using episomal or mRNA reprogramming technologies, 7% of the hiPSC lines were generated with Sendai virus, 2% used circular RNA, and 2% used non-integrating viral vectors (Figure 1G). While all these technologies use the transient expression of OCT4, SOX2, and KLF-4, the technologies vary in the use of oncogenes such as c-myc, L-myc, or TP53 expression. The use of these transcription factors may be a consideration in selecting hiPSC line for translational use.

Conclusion

In the course of developing hPSC-derived products, the selection of the hPSC line as starting material is a critical decision. Understanding the regulatory requirements in the

Table 5. hiPSC line quality systems, regulatory compliance, and available banks for currently available hiPSC lines

Licensor/ distributor		Allele Biotech	Catalent Pharma Solutions	Cedars Sinai Biomanu-facturing	Cellistic	Center for iPS Cell Research and Application (CiRA)	ElevateBio	Fujifilm Cellular Dynamics (FCDI)	LineaBio	Lonza; Applied Stem Cell/ Pluristyx; Applied Stem Cell	Pluristyx	REPROCELL
Regulatory filings	Drug Master File (or similar)	DMF with FDA	no	no	no	NR	no	DMF with FDA	DMF for some lines	DMF with FDA	DMF with FDA	NR
Starting material	primary tissue	skin biopsy	CB	peripheral blood & CB	$CD34^+$ or $CD4^+$ from Leukopak	peripheral blood & CB	CB	PBMC	peripheral blood & CB	CB $CD34^+$	fibroblasts	fibroblasts
	country of origin	USA	Germany & USA	USA	USA	Japan & USA	USA	USA	USA	USA	USA	USA
	donor eligibility compliance	FDA	EU or USA depending on line	USA[a]	USA and EU	USA, EU, and Japan depending on line	USA[a]	USA[a]	USA and EU	USA	USA, EU, and Japan	USA, EU, and Japan
	donor age	30s–60s	neonate	62, 70, or neonate	26 or 29	20s–50s or neonate	neonate	inquire	30s or neonate	neonate	26–60	20s
Reprogramming method	N/A	mRNA	episomal	episomal	viral, non-integrative	episomal or SeV	circRNA	episomal	SeV	Episomal	mRNA	StemRNA
Reprogramming factors	N/A	OCT3/4, SOX2, KLF4, MYC, Nanog, LIN28	not disclosed	OCT3/4, SOX2, KLF4, L-Myc, LTAg, Lin28, shRNA TP53	OCT3/4, SOX2, KLF4, l-Myc	OCT3/4, SOX2, KLF4, L-Myc, Lin28, TP53 (episomal) or OCT3/4, SOX2, KLF4, l-Myc (SeV)	OCT4, SOX2, KLF4, LIN28, NANOG, C-MYC or OCT4, SOX2, KLF4	not disclosed	OCT3/4, SOX2, KLF4, l-Myc	OCT3/4, SOX2, KLF4, L-Myc, LTAg, Lin28, shRNA TP53	OCT3/4, SOX2, KLF4, L-Myc, LTAg, Lin28, shRNA TP53	not disclosed
Derivation/ reprogramming	quality system	GMP	GMP	GMP	principles of GMP	GMP	principles of GMP	GMP	GMP	GMP	GMP	principles of GMP
	xeno reagents	yes	no	yes	yes	no	no	not disclosed	NR	yes	no	NR
Banks available for distribution	quality system	GMP	GMP	GMP & Research	GMP	GMP	principles of GMP	GMP & research	GMP	GMP	GMP	principles of GMP
	xeno reagents	no	no	yes	yes	no	no	no	NR	yes	no	no
	Passage number of available banks	~P10	<P15	P7–P9	P11–P13	P7–P22	Principles of GMP P7, Research P12	contact FCDI	P15	P14	P10, P16	seed bank P6, GMP MCB P9

Not disclosed, distributor did not disclose information due to confidentiality restrictions.
NR, not reported; information was not provided by distributor.
Additional information on unavailable lines can be found in Table S1.
[a]Inquire with provider regarding additional jurisdiction compliance.

jurisdiction(s) where clinical trials and possible commercialization will occur is an important part of this decision. Further, understanding the possible IP limitations and ensuring FTO for the use of the cell line in the desired indications and jurisdictions is a key consideration, especially if commercialization of the hPSC-derived product is intended. Given the acceleration of hPSC product development over the last 2 decades, the availability of off-the-shelf clinically suitable hPSC lines can save resources, time, and costs in progressing these products to patients. Identifying the available materials and providing characterization data as well as information on providers and license contacts eases the process of selection for investigators seeking available materials. While clearly more due diligence must be performed to ensure the suitability of a given line for development of a product in any given protocol, the information presented here represents the most comprehensive and rigorous overview of available hPSC line information to date, includes information that is generally difficult for hPSC-product developers to access, and serves as a valuable starting point and a resource to the stem cell research community as they progress into translational applications.

METHODS

In order to identify hPSC lines derived for clinical applications, comprehensive searches of published papers and manufacturer websites were performed. This assessment was followed by contacting identified hPSC distributors and manufacturers to confirm and broaden the information available regarding the hPSC lines (Table S4). This allowed the collection and inclusion of information that is not currently accessible in the public domain. Data reported here are as received from manufacturing and distributor representatives. Cell lines developed for clinical application but determined to harbor genetic mutations inappropriate for clinical use have been excluded from presentation and subsequent analysis. For presentation, data were separated into lines that are currently available for distribution and those that are not currently available or for which data could not be confirmed.

RESOURCE AVAILABILITY

Lead contact

Requests for further information should be directed to the lead contact, Melissa K. Carpenter (melissa@carpentergroupstrategy.com).

Materials availability

This study did not generate new unique reagents.

Data and code availability

This paper does not report original code.

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AUTHOR CONTRIBUTIONS

M.K.C. and T.E.L. were both responsible for concept, research, and writing of the manuscript.

DECLARATION OF INTERESTS

M.K.C. is the President and owner of Carpenter Consulting Corporation, which provides consulting services for the development of stem cell therapeutics. M.K.C. is named as an inventor on a number of patents related to hPSC manufacturing and product development.

T.E.L. is a full-time employee at WiCell, a non-profit organization that provides PSC lines and characterization services, and is named as an inventor on several patents focused on stem cell culture medium, which are owned by and have been licensed through the Wisconsin Alumni Research Foundation.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

No AI tools were used in the generation, analysis, or presentation of information.

SUPPLEMENTAL INFORMATION

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