Stem Cell Banking

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Different Banks for Different Purposes?

Research iPSC Banks *A celebration of diversity*	Clinical iPSC Banks *A necessity for uniformity*
Maximal genetic diversity of donors	**Minimal genetic diversity of donors**
Normal and diseased donors donor consent for use	Healthy donors only (age may matter) donor consent for use
All forms of variation of interest	HLA differences - Other differences minimised
Different starting cells (cell type)	What is the most suitable starting cell type?
Preparation protocol	**Manufacturing process**
Non-standard and standardised protocols equally valid Multiple labs prepare iPSC Protocols not validated (at best qualified) - gene transfer - protein factor - small molecules?	Validated standard process (GMP) Single process for all cell lines Single or small number of manufacturing sites *Which method?*
Full pluripotency not essential for cell line to be useful.	Consistent pluripotency essential - Failure rate?
Intended uses	**Intended uses**
Basic research Drug discovery/screening/toxicity testing	Treatment of patients

Continued…

Research iPSC Banks *A celebration of diversity*	Clinical iPSC Banks *A necessity for uniformity*
Variable Raw Materials:	**Controlled Raw Materials:**
Research quality raw materials, non-standardised, quality of raw materials varies	High quality raw materials, standardised quality of raw materials essential
Different sources of raw materials used	Qualified suppliers, control of batch variability - supply agreements
Full traceability not essential	Full traceability required
Characterisation	**Quality Control**
	Standard QC
Agreed basic characteristics to define pluripotency	Standard specifications, acceptance criteria, release criteria, stability - How to define acceptance criteria?
Methods and equipment vary between labs - Methods may be qualified/validated within labs but (typically) not between labs. Results from different labs therefore not directly comparable	Validated analytical methods and equipment - Where more than one lab, methods validated between labs Results directly comparable.
Safety Testing	**Safety Testing**
Donor screening	Screen donors/donor history
Limited additional testing as required	Extensive safety testing on resulting cell bank - adventitious agents, TSE risk - Microbial testing
Use of antibiotics possible	No/minimal use of antibiotics

Use of cells from a single bank

Single iPSC line for an allogeneic CTP

Characterisation of reprogrammed cell	Testing differentiated cell-type
Confirm reprogramming complete without abnormalities • Identify nature of any unintended cell changes • Likely impact of any unintended changes on safety • Likely impact of any unintended changes on intended cell function/s* • Identification of any unintended function/s* • Genetic/phenotypic stability • Capacity for stable expansion	Confirm reprogrammed cell can be differentiated into required cell-type • Evidence any unintended cell changes identified due to reprogramming and differentiation don't impact: - Safety (including unintended function/s) - Intended function/s - Tumorigenicity risk Compliance with regulatory requirements for all regions of interest (ideally global)

Bravery, Stem Cells Dev. 2015, 24(1) 1-10

Use of cells from a multiple banks for same product

Multiple HLA-typed iPSC lines for an allogeneic CTP

In addition to those in the previous slide, for all iPSC lines to be used:

Characterisation	Cell line comparability**
Identify any differences between the selected iPSC lines • Likely impact of any differences on safety • Likely impact of any differences on intended (or unintended) cell function/s*	*Confirm all iPSC lines to be used are comparable*: • Differentiation into cell-type of interest • Key intended cell function/s* • Genetic/phenotypic stability • Capacity for stable expansion • Safety (e.g. tumorigenicity, unintended cell functions) • Allowing for inherent variability between individuals