Induced Pluripotent Stem Cell (iPSC) resources - applicant guidance

Since the publication by Yamanaka in 2006 of a method to reprogramme mature cells to a pluripotent state, a growing number of researchers have sought to exploit the potential of such reprogrammed cells, as evidenced by the growing number of iPSC related publications and grant applications to MRC.

This however remains an evolving and dynamic field, which, while offering clear opportunities for progress in disease modelling and drug screening in particular, poses a risk of producing sub-optimally designed efforts that might limit the research and translational utility of derived lines. In light of this risk, the MRC believes that it would be helpful to provide guiding principles on expectations regarding requests for support for the establishment of iPSC resources, with the hope that these principles might also prove of broader value.

Rationale

As when proposing the use of any model system, a strong case needs to be made in support of the proposed iPSCs being able to appropriately recapitulate the natural state or diseased condition of interest versus other means of gaining similar insight.

Sourcing

iPSC collections should ideally be based on **well phenotyped cohorts** with linked clinical and lifestyle data.

Relevant UK regulations and guidelines must be adhered to. For guidance see the Code of Practice for the use of Human Stem Cell lines

Donations should be altruistic, anonymised and traceable.

Appropriate consent must be secured for all proposed uses. To future proof derived lines, consideration should be given to seeking generic consent for a broad range of potential uses, given their pluripotent nature.

Depending on the specific project, consideration should be given to ensuring specific consent is sought for areas of particular interest including:

- Genetic analysis of derived cells
- Potential use in animal research, clinical transplantation or reproductive medicine; and
- Potential commercial applications of cell lines but without donors receiving personal financial benefit
- Consideration should also be given to the feedback of data from derived cell lines.
- The tissue source of cells from which the iPSC lines are derived should be documented and ideally banked for future reference.

Derivation and characterization

This is a fast moving field with numerous derivation approaches in use emerging. Comparable methods of iPSC generation should be used where possible, with full details of the reprogramming method provided.

Lines derived using novel methodologies should be calibrated against lines derived using established protocols and ideally human embryonic stem cell lines. Lines should be characterised to establish features including clonal purity, absence of expression of reprogramming factors, self-renewal capacity, genetic stability and pluripotency. Characterisation should take into account uncertainties regarding the degree of reprogramming and the extent and durability of epigenetic memory.

It is noted that fully characterizing lines may be costly and time consuming. The level of characterisation should be fit for purpose. Robust quality control systems should be put in place to ensure the identity and specification of banked and released cells.

Internationally agreed standards and guidance for stem cell line banking are available through the International Stem Cell Banking Initiative, and advice can be sought through MRC-funded resources such as the UK Stem Cell Bank and Human iPSC Initiative.

Access

Collections should detail how access will be provided to third parties in line with MRC policy on data sharing and cohort resource policy.

Material and Data Transfer Agreements (MDTAs), IP Licensing and Freedom to Operate should be considered, where appropriate, to ensure the broadest utility of derived lines.

MDTAs should control third party use and ensure UK guidelines and ethical procedures are followed, for example in relation to potential use in animals, clinical studies or reproductive science. Equivalent standards should be mandated if exported for overseas use.