

Submission

2016 National Research Infrastructure Roadmap Capability Issues Paper

Name	Mr Mark Shannon
Title/role	General Manager of CellBank Australia
Organisation	Children's Medical Research Institute

Question 3: Should national research infrastructure investment assist with access to international facilities?

In relation to cell and tissue culture models and cell-based therapies and technologies specifically, CellBank Australia believes that national research infrastructure should assist with access to international facilities.

Just over 70,000 immortalised cell lines, naturally-immortal cell lines and finite-life cell lines are known to exist worldwide today. In the health and medical sciences, cultured cell lines are crucial in the study of disease, the discovery of disease treatments, the personalising of treatments, and in the biomanufacturing of cell-based and tissue-engineered products for use as therapeutics. Cell culture is also used in veterinary and agricultural science research.

The next ten years promise to deliver some truly amazing biomedical advances as exciting new cell culture systems continue to be developed. Recent technological developments have given rise to new approaches for the generation of cell models in cancer (examples: 'conditional cell reprogramming' and 'organoids') and when applied to high-purity surgical specimens, the success rates of these are substantially higher than historical methods. Using those protocols, a new generation of cancer cell line models is being developed by overseas consortiums. In addition, new patient derived xenograft (PDX) cancer cell line models are being developed, which mimic the human in vivo tumour microenvironment more faithfully. Furthermore, cultured stem cells (examples: adult stem cells and induced pluripotent stem cells [iPSCs]) are being applied in both disease modelling and in regenerative medicine.

Australian life scientists should be able to access the broadest and deepest range of existing and new cell lines of the highest possible quality from overseas facilities, rather than spend precious resources and time recreating them locally, or worse still, using misidentified or contaminated cell lines obtained from secondary sources. But if done on a by researcher basis, the logistics of accessing high-quality cell lines from overseas facilities can be difficult.

As demonstrated by the continuous operation of cell line repositories across decades in the top 5 life sciences technologies countries of the world, it is much more efficient to have a central importation and distribution vehicle to achieve this (www.phe-culturecollections.org.uk/collections/ecacc.aspx in the UK; www.english.kiz.cas.cn/about/ in China; www.atcc.org in the US; www.dsmz.de/ in

Germany; www.cellbank.nibiohn.go.jp/english/ in Japan). Investment in national research infrastructure should support such a vehicle in Australia.

Moreover, Australian life science researchers need to know how to use cell culture models under Good Cell Culture Practice (GCCP) conditions, for more reproducible research data and more credible research findings. Clinical Good Manufacturing Practice (cGMP) know-how is also needed for the research and development of cell-based therapies and the generation of clinical-grade patient derived cells (example: iPSCs). As demonstrated by national and transnational initiatives that have emerged in the last 10 years, it is much more effective to use central vehicles to provide cell culture best-practices knowledge resources for researcher education and training (examples: www.iclac.org/partners/; www.gbsi.org/work/authenticate/meet-the-alliance/). Investment in national research infrastructure should support such a vehicle in Australia.

Question 5: Should research workforce skills be considered a research infrastructure issue?

In relation to cell and tissue culture models and cell-based therapies and technologies specifically, CellBank Australia believes that research workforce skills should be considered a research infrastructure issue.

Cell culture quality assurance and training are two-sides of the same coin. A recent trans-Tasman survey of cell culture practice found that many of the commonly encountered risks in cell culture need to be better managed (www.onlinelibrary.wiley.com/doi/10.1002/ijc.29817/full). To achieve this, Australia's biomedical researchers need better access to quality-controlled cell lines and quality testing assays and services, and they need better access to training on cell culture best-practices:

- Researchers continue to share their cultures. The majority of respondents obtained cell lines from sources where mycoplasma and authentication testing were not performed routinely.
- Arrangements for mycoplasma and authentication testing are increasingly in place, but many researchers still do not test their cultures. For authentication testing this is particularly true. Of the respondents who did perform testing, 18% reported finding mycoplasma contamination, and 20% reported finding contamination by other cell-lines, in at least one sample.
- 6% of respondents indicated that frozen cell line stocks were lost in the preceding year because of the failure of an on-site liquid nitrogen storage container.
- 10% of respondents indicated that frozen cell line stocks were lost in the preceding year during transit from overseas sources.

Without knowledge resources to support consistency in the provision of biomedical research workforce training in GCCP and cGMP, the progression of ideas through to innovations in Australia will be slowed.

Question 6: How can national research infrastructure assist in training and skills development?

In relation to cell and tissue culture models and cell-based therapies and technologies specifically, CellBank Australia knows of one example where national research infrastructure has assisted in training and skills development.

Since 1990, the European Collection of Authenticated Cell Cultures has assisted in cell culture training and skills development (www.phe-culturecollections.org.uk/services/training/training.aspx). Investment in national research infrastructure should support such a vehicle in Australia.

Health and Medical Sciences

Question 15: Are the identified emerging directions and research infrastructure capabilities for Health and Medical Sciences right? Are there any missing or additional needed?

In the health and medical science capability area, the 2016 Roadmap Issues Paper highlights the need for an integrated national program of research infrastructure to support research and development of biologics, novel therapies, bioengineering solutions for precision medicine, and stem cell therapies. **CellBank Australia agrees that such a program to support the research and development of cell-based therapies and personalised medicine is indeed required, but thinks that basic laboratory research needs to be supported by that program as well.** Thus, more correctly in our view, an integrated national program of research infrastructure to support cell and tissue culture models and cell-based therapies and technologies is needed.

Question 16: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

In relation to cell and tissue culture models and cell-based therapies and technologies specifically, CellBank Australia knows of a number of international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond.

Australia's engagement in international research infrastructure includes a number of dimensions, one of which is "having a seat at the table" and another is researcher access. CellBank Australia highlights the following initiatives in that broad context:

- Human Cancer Models Initiative - an international effort to develop 1,000 cancer cell models that better represent the hallmarks and diversity of human cancer (www.sanger.ac.uk/science/collaboration/human-cancer-model-initiative-hcmi).
- International Stem Cell Initiative - a worldwide collaborative effort to establish a consensus on basic criteria and techniques that will underpin the eventual development of applications for stem cell lines (www.stem-cell-forum.net/initiatives/isc/).

- The ISCF Stem Cell Banking Initiative (ISCBI) - co-ordinated by the UK Stem Cell Bank, ISCBI aims to create a global network of stem cell banks through support for existing banks and by encouraging the development of new banks in member countries (www.stem-cell-forum.net/initiatives/international-stem-cell-banking-initiative/).
- Cell Authentication Alliance - an international alliance that brings together a diverse set of committed stakeholders with the sole purpose of making routine cell line authentication standard practice as part of quality biomedical research (www.gbsi.org/gbsi-content/uploads/2015/12/Cell-Authentication-Alliance-12.15.15v3.pdf).
- International Cell Line Authentication Committee - an international effort to make cell line misidentification more visible and to promote awareness and authentication testing as effective ways to combat it (www.iclac.org/).
- GCCP 2.0 Collaboration – an international initiative that seeks to update the 2005 Good Cell Culture Practice document (<http://caat.jhsph.edu/programs/GCCP/index.html>).
- Health and Environmental Sciences Institute Genetic Toxicology Technical Committee – a technical committee that seeks to improve the scientific basis of the interpretation of results from genetic toxicology tests for purposes of more accurate hazard identification and assessment of human risk (www.hesiglobal.org/genetic-toxicology-gttc/).
- Cancer Cell Line Factory initiative - an international effort to establish >10,000 cancer cell line models as a community resource (<http://www.nature.com/nrg/journal/v16/n7/full/nrg3967.html>).

Other Comments

CellBank Australia understands that Australia's national research infrastructure must deliver a national benefit and should also have an impact on the world stage, and welcomes the opportunity to make this submission on the 2016 National Research Infrastructure Roadmap Capability Issues Paper.

As Australia's sole national not-for-profit cell line repository, CellBank Australia is a unique and essential piece of Australia's national research infrastructure. The primary purpose of CellBank Australia is to make it cheaper and easier for researchers to access high quality cell lines and cell culture related services. CellBank Australia distributes 1,800 cell lines for the European Collection of Authenticated Cell Cultures (ECACC) to Australian and New Zealand researchers. In turn, CellBank Australia's own cell lines are distributed by ECACC outside of Australia and New Zealand. Information about CellBank Australia's other services can be found at www.cellbankaustralia.com.

CellBank Australia hopes that this submission is of assistance. If the 2016 Roadmap Expert Taskforce wish to discuss the matters raised further, the General Manager of CellBank Australia is available for input and discussion.