Brave new world

How beauteous mankind is! O brave new world that has such people in't![1]

We all agree on two things. Managing human biological samples is and always has been an essential part of biomedical research. And this activity, biobanking, has to be paid for.

Where disagreement has existed is over what mechanisms might best ensure that supply meets demand. Some have faith in market mechanisms. Others don't. The only way to resolve this is to put it to the test, to look at the evidence.

All the biobanks that have recently described their financial models in the pages of *Biopreservation and Biobanking*[2 3 4 5 6 7 8 9] and virtually all those analysed by Technopolis[10], BETA[11] and now in these pages by Gee *et al.*[12] were constructed, filled with samples and then maintained using public (including charitable) funds.

Despite the passage of decades, there are no examples of biobanks that have been constructed, filled and maintained using market mechanisms alone. Gee *et al.* identify in this issue features of market failure in biobanking. In-house corporate biobanks provide a simple proof of the point: these biobanks supply most of internal demand for samples as a not-for-profit service. It's not that corporations have missed a trick to improve the bottom line. It's that they have faced reality – while demand is substantial, the prospects of profits are dim.

What is so bizarre is that many public research funders have not faced up to this reality. Yes, they fund construction of a biobank that manages the samples that are to be used for the research that they concomitantly fund. But then they hanker after achieving zero maintenance costs and urge adoption of "cost recovery" schemes.

These schemes are inefficient: they recycle public money unreliably, unpredictably and with full transaction costs (e.g. accountants' costs). To survive, the schemes need continuous subsidy – using more public money.

Without the funding of its maintenance, CERN would have been closed down once the 'God Particle' had been found. Or the UK's Genome Campus would have been closed down once it had finished its share of the human genome sequence.

Why do funders recognise that management of all the data associated with samples is an ongoing, long-term cost, but do not recognise this for the samples themselves? Why is Big Data good but Big Samples bad? The answer is that funders know that we researchers will duck and weave to get those samples and keep them. We will collect them and we will store them by hook or by crook, come what may.

Even today, you may well collect samples, say, for a genetic disease, dipping into whatever funds you can. You may even pay out of your own pocket. That's how desperate researchers often are. Once we have collected them, we squirrel them away. And, here's the rub, our maintenance costs are very well hidden, as Gee *et al.* report.

But two things have changed the game: the internet and the human genome sequence. At a stroke, it became both possible and necessary to undertake studies on human samples on a far bigger scale.

Before the genome sequence was even complete, big money was on offer for the first time to support sample accrual. In the late 1990's the UK's medical research agency (MRC) provided $12m to 14 consortia each wanting to study the genetic epidemiology of a high-impact disease by collecting blood

from sometimes thousands of cases and controls. The UK was blazoning the trail. This was the start of the new Big Biology that the Human Genome Project was promising.

To support this, the agency also proposed construction of a network of half a dozen biobanks across the country to undertake the management of future research samples and to promote their best possible use. The UK, it seemed, had 20:20 vision and, as a result, genes associated with high impact diseases were pinpointed in double fast time[13].

UK biobanking policy mirrored OECD's contemporaneous recommendations on biobanking[14]. Contemplating the biotechnology needs of 21st century economies, the world's leading economic think tank said:

> *"To realise the benefits of BRCs [viz biobanks], each [OECD] Member country should consider developing a policy for BRCs that recognises their value. This policy may be co-ordinated across ministerial departments and other funding bodies, and should take into consideration collaboration and financial support for national, regional and international facilities.*
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> *"This policy should encompass service centres, generalised as well as specialised collections, associated data sets, bioinformatics systems, as well as the acquisition, evaluation and dissemination of information and materials, all of which are important aspects of BRCs."* (p51)

But, in the upshot, a national biobank network (as a distributed research infrastructure) was abandoned in the UK and OECD's prescient 2001 report was left to gather dust. Why did this happen? We need to answer this if current national and international efforts to construct biobank networks are to succeed.

The answer is shocking and far-reaching: biobanking is a disruptive technology. Its implications and consequences reach far beyond the technology itself. It threatens the *status quo* in established biomedical research behaviour and practices. Neither OECD nor anyone else has explored this fully.

Here is an initial attempt to do this. We researchers have established our careers by first acquiring resources. We treat the samples that we have collected as ours alone. We alone manage them. If they were to be managed in any other way – by a biobank with its governance arrangements and its access policy – we will fear that we may lose control.

Such loss of control poses severe risks. If I, a lonesome researcher, want to win a grant, then I really need to "own" the necessary samples. If I do, my grant proposal will be stronger than that of a competitor who lacks samples (and hence lacks adequate statistical power). In other words, if I want to win a virtuous competition of ideas, I must first win a venal competition for samples (other things being equal).

Most will recognise that competition on ideas is virtuous. But we fail, by and large, to recognise that competition for research samples is venal, at least when the materials have human origin. The problem is that the altruistic donor provides a sample not to enhance my career prospects but to enable the best possible research to be undertaken. The donor helps the former and, unknowingly, may fail to enable the latter. By contrast, from the researcher's point of view, there is no problem: he or she has won a peer-reviewed grant. It was the best proposal.

Biobanking tends to disrupt this long-standing linkage of resources and ideas: it reduces competition for samples and thereby enables greater competition between ideas. This is precisely what the UK Biobank project's access policy[15] promotes. Disruption is all the greater when a biobank network is formed because in a world of biobanks and networks, I no longer have absolute control of the human samples altruistically provided by donors. I therefore compete with my fellow researchers primarily by using my brain. I need not be beauteous, but I must be exceptionally brave in this new world.

But it gets worse. If there is a network, then I shall be obliged eventually to work collaboratively. I shall be forced to share my ideas before publication. I will end up on multi-author – *ergo* low-impact – papers. I will think bitterly: "It may be better research I am doing, but what about my status?"

This brave new world of biobanking is a world upside down: biobanking is a missile aimed at the fabric of our profession. It prompts far-reaching change to the biomedical research profession, how we are assessed, how our institutions are assessed and funded, how they interact with other institutions. This is a shocking conclusion. No wonder nearly all biomedical research funders globally have hesitated to maintain this dangerous technology since it was proposed by OECD.

But is there any alternative in the new world of Big Biology? Networked biobanking is essential to it. It is essential for enabling stratified /precision / personalised medicine. It is essential for effective biomarker discovery. And, beyond basic research, it is essential for evidence-based interventions to improve the health of populations. In other words, biobank networks are a necessary part of the fabric of both health research and health delivery. Once we have them, they will be here to stay.

However, networks will not be fully sustainable until we begin to adapt our institutions and accept that, for the foreseeable future, we cannot thrust upon the market what the market has persistently failed successfully to exploit. While biobanking remains an intrinsic part of research, it is a public good in whose provision the state must play some role[16].

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References

[1] Shakespeare W. The Tempest. Act V. Scene 1.
[2] Riegman PHJ. From AAA+ to BB− and on the Way Back Again. Biopreservation and Biobanking. 2014;12:292-293.
[3] Barnes RO, Schacter B, Kodeeswaran S, CTRNet Management Committee, Watson PH.Funding Sources for Canadian Biorepositories: The Role of User Fees and Strategies to Help Fill the Gap. Biopreservation and Biobanking. 2014;12:300-305.
[4] Wilson GD, D'Angelo K, Pruetz BL, Geddes TJ, Larson DM, Akervall J. The Challenge of Sustaining a Hospital-Based Biobank and Core Molecular Laboratory: The Beaumont Experience. Biopreservation and Biobanking. 2014;12:306-311.
[5] Matharoo-Ball B, Thomson BJ. Nottingham Health Science Biobank: a Sustainable Bioresource. Biopreservation and Biobanking. 2014;12:312-316.
[6] Albert M, Bartlett J, Johnston RN, Schacter B, Watson P. Biobank Bootstrapping: Is Biobank Sustainability Possible Through Cost Recovery? Biopreservation and Biobanking. 2014;12:374-380.
[7] Parry-Jones A. Assessing the Financial, Operational, and Social Sustainability of a Biobank: The Wales Cancer Bank Case Study. Biopreservation and Biobanking. 2014;12:381-388.
[8] Warth R, Perren A. Construction of a Business Model to Assure Financial Sustainability of Biobanks. Biopreservation and Biobanking. 2014;12:389-394.
[9] Carpenter JE, Clarke CL. Biobanking Sustainability—Experiences of the Australian Breast Cancer Tissue Bank (ABCTB). Biopreservation and Biobanking. 2014;12:395-401
[10] BBMRI: an evaluation strategy for socio-economic impact assessment. A report for BBMRI WP1/WP7. Technopolis. 21 September2010.
[11] BETA, CNRS and Universite de Strasbourg .Health and Economic Impact of BBMRI; Evaluation methodology and access rule so biobank networks. Final report – Deliverable D5. May 2010.
[12] Gee S, Oliver R, Corfield J, Georghiou L, Yuille M. Financing UK biobanks: rationale for a National Biobanking Research Infrastructure. Biopreservation and Biobanking. 2015 (this issue).
[13] Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature. 2007;447:661-78. PMID: 17554300
[14] OECD Biological Resource Centres: Underpinning the future of life sciences and biotechnology. Paris. March 2001. ISBN 92-64-18690-5. www.oecd.org/sti/biotech/2487422.pdf
[15] http://www.ukbiobank.ac.uk/using-the-resource/

[16] Stiglitz JE. Knowledge as a Global Public Good in Kaul I, Grunberg I, Stern MA (eds). Global Public Goods: International Cooperation in the 21st Century. 1999. Oxford University Press, USA. ISBN-10: 0195130529; ISBN-13: 978-0195130522.