Rising without trace

The folks of the lab have been taking a greater-than-usual interest in museum visiting recently, specifically the amazing National Museum of Scotland located in Chambers St, Edinburgh. The (admittedly narcissistic) reason for our current enthralment with the place is that the new technology gallery has just opened and it contains, amongst its many exhibits, one of our tissue-engineered mini-kidneys. It is not the first that we made, for reasons explained below, but it is representative of the earliest ones we could make and is for this reason already obsolete.

The experience of working with the museum staff has been a very interesting one, and Sophie Goggins in particular was generous with her time and very open in explaining the demands of her job. What she said made me understand something I had been too unobservant to notice before.

The duty of museum curators is to try to preserve carefully chosen artefacts that represent the story of the country's developing culture, 'culture' here including science and technology as well as art, sport, furniture, crockery and all of the other things one would expect in a major museum. As a leading centre of Enlightenment thinking, Edinburgh has a wealth of scientific artefacts from the eighteenth and nineteenth centuries. There are microscopes, telescopes, pieces of surgical equipment, anatomical models, lethal-looking pieces of electrical apparatus, fossils, rocks, stuffed animals, dried plants and… well, come and visit some time and allow a few days if you want to visit all of the scientifically and medically relevant museums in the city. Georgian and Victorian scientists built a lot of kit, which they looked after long-term, and many of the objects of their study were tangible enough that they would be found lurking in drawers years after the scientist concerned had gone. In short, these old pioneers were a museum curator's dream.

What I had never noticed until listening to Sophie is that 21st-century scientists are, by and large, a curator's nightmare. In the biosciences, in particular, we leave almost nothing behind. Much of our kit is commercial and lasts for a tiny fraction of the life of Victorian equipment, not because it is badly built but because it needs spares and servicing that its manufacturers cease to provide after, sometimes, as little as a decade. Even completely novel, hand-made equipment, which may turn out to the foundation of a new technology, tends to be taken apart and recycled as soon as a neat commercially built version comes along. This is driven by the fact that lab space is at a premium and the Heath Robinson-style individual components used for the prototype may be needed for making a prototype for some other product of the inventor's fevered mind. By the time a museum curator comes to make enquiries, nothing remains beyond the scorch marks in the ceiling. Furthermore, much of the work of modern biology is at the cellular level. When we study cell-level anatomy, we typically use fluorescence-based stains and reporter genes and photograph them immediately. We have to – these methods of visualization are strictly temporary and degrade in hours or, at best, weeks. Molecular analyses are again done on gels that are temporary, photographed digitally, then thrown away. I could go on, but the other examples would only reinforce the general point that the output of most of modern biology is a bunch of bits on a computer, representing images, DNA sequences, cell counts etc.

The way most of us are working, we threaten to leave very little behind to mark our brief contributions to the history of science. The papers we publish will be there for sure (or rather, in many journals, the digital representations of 'papers' will be there because a printable pdf is as close as those journals get to actual dead trees). We will, however, leave almost nothing of what we actually handled, touched, cared about. One does not have to be a curator to feel concern about this: the Victorians were great, but surely our time deserves to be remembered too. It would be shame if our technologies were to rise without leaving a trace for others to see.

The good news is that, with a little imagination, it is possible to preserve even biological experiments for posterity, or at least to make preservable versions of something that might turn out to be an important advance. Doing so regularly on the assumption that a major museum will want it would, I admit, seem impossibly arrogant (and we would not have dreamt of doing so until the National Museum came to us), but keeping artefacts to build up a display of the life of a university department is altogether more reasonable and, of course, it means that the material will exist should someone want to display it elsewhere.

In our case, the museum wanted an example of one of our early kidneys that had been engineered from simple suspensions of mouse renogenic stem cells. Our problem is that we had only digital images to offer, because we had used fluorescent staining for all of the analyses in our publications, and had kept the images and disposed of the fast-degrading and tiny engineered organs. The challenge was to make a stable version for the museum, a version that was stained in a way that would allow its inner structure to be viewed under a normal lens or school-type microscope, and that would be stable for many years. We (I was doing all of this with my talented colleague, Dr. Melanie Lawrence) therefore had to find a new stain and some method for stabilization.

Conventional stains used, for example, in standard hospital labs are very good at staining all tissues but they are designed to be used on thin sections. For a three-dimensional entity, even one as small as our little engineered kidneys, the stains just turn everything purply-black and all inner structure is obscured (guess how we know…). To show just the tubes inside the kidneys, we still needed to use antibody-based staining methods but needed not to rely on antibodies themselves for the long-term stability of the stain when the sample was in the museum. The solution came from a hybrid staining protocols used for two other techniques, electron microscopy and Western blotting. Electron microscopy is good at detecting metals; the 'stains' used for electron microscopy often contain metals and when electron microscopists want to use antibodies, they chemically attach to them tiny particles of gold. We experimented with gold-labelled antibodies on our kidneys, but the image the very fine gold particles produced was very faint under a normal light microscope – just a faint pink hue along the edges of the tubules. The contrast was just about acceptable for research but would have been useless for a museum. Then, I remembered my graduate student days, probing Western blots of proteins on nylon membranes with gold-labelled antibodies and adding a second step to precipitate silver on both the gold and on any already-precipitated silver. This reaction feeds on itself and can generate very strong staining. Applied to the kidneys, it worked: the bulk tissue of the organ remained transparent and the tubes within stained deep brown, their membranes becoming coated with metal that ought to last for a very long time indeed.

All that remained was to mount the kidneys on a solid glass support (for which we used a thick glass slide) and to seal them in. For this final operation, I followed along-standing tradition of my own scientific papers (the ones for which I actually do the bench science), which is to specify in the Materials and Methods section a slightly ridiculous ingredient that I really did use. So far, no

journal editor has vetoed any of these; either they do not notice, or more probably they share my feeling that scientific writing can include a little humour. That is why the edges of the cover glass of the museum specimen are, like the slides of so many of my real experiments, sealed with bright nail-varnish (*Minxy Pink*, if you are interested). The source of the colour gets no mention in the catalogue entry: it will just have to be a puzzle for posterity.

Jamie Davies,
Edinburgh,
July 2016

Links:

National Museums of Scotland: http://www.nms.ac.uk/national-museum-of-scotland

Catalogue entry for our kidney: http://www.nms.ac.uk/explore/collection-search-results/?item_id=723254