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The democracy carousel

European law has allowed citizens to force a debate on human embryonic stem cells less than a year after the previous one. This fruitless democratic exercise has left scientists spinning in uncertainty.

Winston Churchill famously said that democracy was the worst form of government, except for all the others. Scientists in the European Union (EU) who work with human embryonic stem cells have more reasons than most to see the systems's flaws. Yet again, they have been forced to discuss and defend the purpose and ethics of their work. Once more, they must watch as possible curbs on their research are proposed.

The trigger this time is the latest in a series of European Citizens' Initiatives (ECIs): petitions that were introduced in 2012 and that automatically prompt a formal public hearing in the European Parliament when they reach more than 1 million signatures across at least seven EU countries. The 'One of Us' petition, which was signed by more than 1.7 million people across all 28 EU countries, calls for a ban on financing any activity that requires the destruction of human embryos, directly or indirectly — so in addition to forbidding EU funding for work on human embryonic stem cells, it proposes a block on aid for agencies that offer abortion advice.

If this topic sounds rather familiar, that's because the same sensitive issue was extensively discussed by the European Parliament in 2006, and again in 2013, before the launch of the multi-billion-euro Seventh Framework and Horizon 2020 research programmes, respectively. In both cases, and after wide consultation, the EU decided to fund such research, provided that approved projects used existing human embryonic stem-cell lines and respected Europe's variable national laws. Yet, in a hearing on 10 April, the European Parliament dutifully rehearsed the same arguments that had led to its previous decisions.

The atmosphere in the crowded auditorium was less decorous than European parliamentarians are used to. Scornful booing erupted, for example, when the parliament's legal-committee representative, Françoise Castex, declared that there was no reason in law to stop funding human embryo research.

The European Commission must prepare a report responding to the One of Us initiative before 28 May, addressing whether any EU legislation could or should be changed in response. It should not.

European scientists have been unsettled by the One of Us initiative, and also by the prospect of a parliamentary hearing of another ECI, 'Stop Vivisection', that calls for the 2010 legislation on the use of animals in research to be replaced by a new directive banning all animal experimentation. That hearing is likely to take place in September.

What is the value of these new efforts in participatory democracy? The general aim sounds noble; it is, of course, good to be able to hold power to account and to involve citizens in setting agendas for discussion. But in practice, and certainly in the case of these two initiatives, they have little democratic merit. The uses of human embryonic stem cells and animals in research have both been discussed very recently. The 2010 animal legislation represented a hard-fought-for compromise that was agreed by EU member states and the European Parliament only after more than a decade of debate involving consultation with all sides. The even-more-recent legislation on funding of research with human embryonic stem cells also represents a compromise in which all sides, including the representatives of One of Us, had their say. To allow a group representing less than 0.4% of the EU's 500 million or so inhabitants to reignite the debate after such a short time seems more of an anti-democratic act than an enlightened one. Worse, the commission's report will of necessity have to repeat the arguments that led to the 2013 decision to fund some research using human embryonic stem cells, again reflecting that a majority supported the compromise. That opens the door to allegations that the EU invites ECIs — and then ignores them.

"What is the value of these new efforts in participatory democracy?"

ECIs are here to stay. The European Commission is quick to point out that they do not represent direct democracy — there is no obligation to change rules in response to them, unlike the recent Swiss referendum curbing immigration, which is now making great difficulties for scientists (see *Nature* **506,** 277; 2014). But they still create an undesirable atmosphere of uncertainty. They mean that researchers will have to increase their efforts to keep the achievements of science in the headlines.

When it comes to complex, highly emotional issues, passionate minority groups can easily and quickly drum up well-supported petitions in a way that scientists cannot (although patient groups could, and perhaps should, think about doing so). Scientists and advocates can, however, build a counterbalance by continuing to present their work as necessary to the well-being of all members of society — however they may vote. ■

Cancer crossroads

Efforts to understand cancer genomes should take on a fresh focus.

Since the discovery of the first cancer-causing genes in the 1970s, researchers have been eager to catalogue the mutations that can cause cancer. Each mutated gene holds the potential to expand our understanding of what causes the disease — and how to treat it.

The latest progress towards that goal was on display last week, when 18,400 people descended on San Diego in California to attend the annual American Association for Cancer Research meeting. Researchers showed how patterns of mutation can be used to track down the agent that caused them — sunlight, for example, leaves a footprint that differs from a cancer-causing viral infection. Another team had

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catalogued cancer-associated mutations in patients with advanced melanoma, hoping to use the information to tailor immune cells to destroy tumours. And promising initial results were unveiled on targeting a protein called IDH2, mutations in which crop up in many different tumour types (see *Nature* **508,** 158–159; 2014).

It has taken a massive effort to make such achievements possible. Seventeen countries have invested in sequencing cancer genomes through the International Cancer Genome Consortium (ICGC), which aims to sequence more than 25,000 samples. The largest and oldest component of that project is The Cancer Genome Atlas (TCGA) at the US National Cancer Institute (NCI) in Bethesda, Maryland, which intends to characterize 10,000 tumours.

TCGA was initially controversial, because researchers worried that the project would direct funds away from grants to individual investigators. Early results — which showed that cancer mutations were much more abundant and diverse than expected — even evoked schadenfreude in some circles (see *Nature* **455,** 148; 2008). Criticism died down as the project bore fruit.

But TCGA is now winding down: the project ceased collecting new tissue samples last December. The ICGC, too, has virtually stopped accepting proposals for new projects. TCGA aims to complete sequencing and further characterization of its cancer samples by the end of the year. After that, a few groups will receive funding to analyse the data for the next two years. But the programme, as it existed, will cease.

Some cancer researchers have advocated that the programme should continue. Stopping now would be premature, their argument goes, because we have yet to achieve a comprehensive catalogue of cancer-causing mutations. A study published earlier this year determined that compiling a list of mutations present in at least 2% of cancers would require sequencing of about 2,000 tumours in each of at least 50 tumour types (M. S. Lawrence *et al. Nature* **505,** 495–501; 2014). For most cancers, we are still far short of that goal.

On a more optimistic note, the end of the older projects should herald a needed transformation in the field. When TCGA and the ICGC were launched, the technology dictated that only fresh tumour samples could be sequenced. That restriction limited researchers' ability to link sequencing data with clinical outcomes because that information might not be available until years after the sample was taken. Also, at that time, oncologists did not take more than one biopsy of a tumour from a patient, which limited studies of how tumours changed during and after treatment, and how metastases differed from primary tumours.

"The end of the older projects should herald a needed transformation in the field."

Those hurdles have now been largely surmounted. Improved techniques allow researchers to sequence DNA collected from tissue preserved in formaldehyde and embedded in paraffin, opening the door to using banked samples with linked clinical data. And although still an uncommon practice, several clinical trials have shown that many patients are willing to submit to extra biopsies.

To replace TCGA, the NCI intends to sequence tumours from patients enlisted in some of its clinical trials. Other teams will no doubt do the same, allowing researchers to learn more about the importance of a given mutation by associating it with the response to therapy or to overall prognosis.

These changes require a new mindset. Clinical researchers will need to change consent forms for donation of tissue samples, to allow the association of clinical data with the sample. They will have to collect their samples using protocols that ensure utility not just for classical pathology but also for sequencing. Data security, always a concern when dealing with patient information, will need to be bolstered.

Nevertheless, to continue the work is a worthy undertaking. The end of TCGA also represents an opportunity for the field to balance its cancer-genomics projects more evenly between cataloguing mutations and studying their functional significance. Functional studies have had short shrift, whereas sequencing — a simple concept, and easier to communicate to policy-makers and the public — has taken the lead. Correcting that imbalance will lead to exciting discoveries for science and for patients. ■

Practical nonsense

Downgrading practical science will impede UK students in the global workplace.

"Equipped with his five senses, man explores the universe around him and calls the adventure Science." So wrote US astronomer Edwin Hubble in 1929, but was he right? How much should science be an exploration of the senses — as well as a test of knowledge and intellectual flexibility? Does a physics student need to peer through a telescope to grasp the enormity of the Universe? Must a potential chemist grapple with the tap of a titration flask to appreciate the subtleties of reaction synthesis? The UK government is about to take a massive — and massively misguided — gamble that they do not.

Education officials in Britain have decided to remove assessed practical work from the landmark A-level qualification, taken by students aged 16–18 and a prerequisite for university. In doing so, the officials and the school science they oversee have taken a huge step backwards. The move could see an entire generation denied the opportunity to develop an interest in the practical experience of doing science.

The Office of Qualifications and Examinations Regulation (Ofqual), which has made the change, says that such fears are overblown. Practical skills will still be tested, it says, and the results presented as a separate pass/fail mark to accompany the existing A-level letter grade. Schools will be inspected. Practical skills, Ofqual promises, will survive.

There are two problems with this. First, as institutions told Ofqual when it floated the idea last year, universities will still focus on the mark — how else will they differentiate between the thousands of applicants? Second, if the result of a practical test is seen as secondary to the overall grade, then schools will be less concerned with it. UK education has become a ruthless marketplace in which schools are judged by how well they can shift students on to the next stage. Anything that interferes with that is unlikely to be a priority. Students, especially those at poorer-performing schools, will simply be offered fewer lessons in practical science.

As John Baruch pointed out in a World View article last month, the UK change comes at a time when other nations, China chief among them, are placing increased emphasis on practical skills in school-leaving exams (see *Nature* **507,** 141; 2014). The United Kingdom is poised to send its science students into the global competition for scientific and technical jobs with one arm tied behind their backs.

Ofqual made its decision in the face of fierce criticism from leading scientists and science advocates. There were certainly problems with testing practical skills through coursework — long viewed by students as the soft underbelly of academic assessment — but, in this case, the proposed solution is worse. As Imran Khan, chief executive of the British Science Association, puts it: "You wouldn't dream of assessing other practical subjects — like languages, music, or design — by a written test alone, and the same should be true of science." We are back to Hubble's five senses, and the need to stimulate and extend them.

Practical experiments teach the reality of science, with all its frustrations and rewards. The real world, after all, does not always proceed smoothly. As the old joke among physics teachers goes: if an experiment smells, it is chemistry; if it moves, it is biology; and if it doesn't work, it is physics. ■

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