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Prove the worth of basic research

European agencies are backing fundamental science and working to prove that it pays off. Other national and international bodies should follow suit.

The happy accidents that come from blue-skies research are gold dust for scientists, and help them to push back against political demands for applied work. Who doesn't know by now that we have basic research to thank for the World Wide Web? Who hasn't heard that curious researchers trying to work out how bacteria biochemically tick stumbled on the CRISPR–Cas9 gene-editing techniques that have gone on to transform biotechnology?

Still, political support for a thriving fundamental research base cannot be taken for granted. So two unexpected — and quite different — moves announced this month are worth noting and celebrating.

On 15 July, the hard-nosed European Investment Bank, which lends with favourable terms to European Union member states to support EU policy objectives, gave a massive loan to Greece to start up an agency for basic research. This not only provides a much needed moral boost for Greece, which has had to live for years with the label 'credit-unworthy', but it also sends a crystal-clear message to politicians around the world on the clear importance of pure science to a secure economic future.

Then, at the biennial European Open Science Forum in Manchester, UK, on 26 July, European Research Council (ERC) president Jean-Pierre Bourguignon announced that the council will start to monitor the outcomes of the research it funds. The ERC, which was founded in 2007 and awards sought-after grants that confer immense prestige on recipients, aims to systematically build a body of evidence to demonstrate the value of pure research beyond well-celebrated examples such as those mentioned above.

In the past 18 months, the ERC has quietly carried out a pilot effort to evaluate 199 of its first completed projects. It did not take the easy option of just looking at bibliometrics. It wisely took the more informative but more difficult option of asking experts not to get hung up on numbers, but to make judgements based on their expertise. They had to grade the scientific success of each project and assess its impact on the world outside science.

The results? The ERC seems to be a resounding success. (Although most of the reviewers had worked with the council before and so can't be classed as wholly independent.) Almost three-quarters of the projects were judged to have generated a scientific breakthrough or major scientific advance, and one-quarter had — or might have in the future — an impact on the economy, society or policymaking. The exercise cost a mere €200,000 (US$220,000), a tiny fraction of the ERC budget.

This is a very small qualitative study that has some flaws (see page 477), and the results cannot be extrapolated to the 6,000 or more grants, worth €9.8 billion, that the ERC has so far paid out. But the evaluation process is itself under constant review and many of its flaws should be ironed out in future rounds.

The results of the pilot will surprise few scientists, given the well-honed and widely admired selection procedures of the ERC. But as the years go by, they will add up to a convincing portfolio to present to politicians, showing that ERC spending on basic research is not wasted — it usually leads to scientific success, which in turn often leads to positive outcomes for society.

This type of retrospective audit is rare. And it is perhaps surprising that national research agencies around the world do not do it. The DFG in Germany, for example, feels that its own selection processes are reliable enough not to require further proof of this type — but then, in Germany, basic research is unusually well protected from the vagaries of politics. The time may be ripe for a modest investment like the ERC's to be more widely applied.

"The struggle between politicians and fundamental researchers is eternal."

The struggle between politicians and fundamental researchers is eternal, and understandably so. In democracies, politicians have to demonstrate to their electorates every five years or so that they have presided over serial successes and have not thrown away taxpayers' money on self-indulgent frippery. The scientific community has to find ways to continually show them that it is producing some of the successes. The strong endorsement of basic research by the European Investment Bank is a useful card that can be widely played to this end. And the ERC's example is one to follow: gather evidence for the worth of evidence-based arguments. ■

Cures for all

US lawmakers should give drug firms the confidence to test cancer therapies in children.

A cancer diagnosis is a shock, but adults with the disease can take some comfort in the numerous treatments available to them — both through clinical trials and as drugs that are already on the market. Children cannot. Because they make up only 1% of US patients with cancer, children are a low priority for pharmaceutical companies that want to launch an effective drug quickly. The hassle of a paediatric clinical trial may not seem worth it until after the drug has proved to be safe and effective in adults. This process can take decades, leaving children with therapies that are sometimes almost obsolete.

To access therapies early, parents of these children can turn to compassionate-use programmes, in which companies give experimental drugs to people who are in desperate need. In the United States, firms that agree to provide medicines in this way will ask the Food and Drug Authority for emergency permission, which is almost always granted.

This system, although helpful for some, is rife with complications.

Patients and their families report difficulties in applying for such programmes, and say that they rarely receive responses. Companies that withhold a drug — because it is in short supply or not right for a patient — can find themselves on the receiving end of critical social-media campaigns highlighting individual patients. And firms worry that if a person dies or is harmed while taking a drug, it could hurt the drug's chances of being approved. No one knows how many requests parents make and how often companies approve them, but anecdotally, firms often deny drugs on the grounds that they have not been tested in children.

Proper clinical trials for childhood cancer drugs are scarce. Designing a clinical trial is never simple, but adding children to the picture complicates the process immensely. Children are not just 'small adults' — they metabolize drugs in very different ways. It is difficult to predict from adult or animal studies whether a chemotherapy drug will be more or less toxic in a child, and at what dose. The process of obtaining informed consent for children participating in a trial can also be more complicated. And companies fear that the death of a child — even if unrelated to the treatment — could bring bad publicity for a new drug.

Recent years have seen attempts to make more drugs available to treat children. In the United States, a 2003 law known as the Pediatric Research Equity Act (PREA) requires that companies develop a plan for how they will test experimental drugs in children, although many trials are exempted. A second law, called the Best Pharmaceuticals for Children Act, motivates companies to perform paediatric clinical trials by granting an extra six months of market exclusivity for the adult drug.

Overall, these laws have been successful, leading to hundreds of drug labels being updated with information for use in children. But legal loopholes often prevent children with cancer from accessing new drugs. For instance, therapies for conditions that do not affect children — such as Alzheimer's disease — are exempt from the PREA. And exemptions intended for such diseases have been broadly applied to cancer. For example, therapies that are being trialled in adults with breast cancer are exempted because children do not get that cancer, even if the drug could treat a childhood cancer in a different organ.

Also exempted are drugs for 'orphan' diseases that affect fewer than 200,000 people in the United States. The number of orphan designations has skyrocketed in recent years — the improved ability to define the molecular basis of an individual's cancer means that diagnoses have become increasingly subdivided, and the majority of approved cancer drugs now carry this orphan designation.

"Legal loopholes often prevent children with cancer from accessing new drugs."

Legislation is now attempting to close those loopholes. The Research to Accelerate Cures and Equity (RACE) for Children Act, introduced to the US Congress on 14 July, would require companies to apply the PREA to any therapy with a molecular target that is relevant to both an adult and a childhood disease. It would also end the exemption for orphan diseases. Last July, the European Medicines Agency passed similar rules to make it more difficult for companies to avoid testing drugs in children. This applies when the disease has a common mechanism in adults and children, unless the drug is likely to be unsafe in children.

With Congress now out of session and focused on the upcoming US election, the RACE for Children Act is unlikely to advance before next year. But when lawmakers pick it up, they should also address problems with compassionate-use programmes — and ensure a transparent and useful process for people to gain access to unapproved drugs. They should also encourage companies to make more drugs available through market incentives, and provide increased protection should something go wrong. ■

On impact

Nature *and the Nature journals are diversifying their presentation of performance indicators.*

Metrics are intrinsically reductive and, as such, can be dangerous. Relying on them as a yardstick of performance, rather than as a pointer to underlying achievements and challenges, usually leads to pathological behaviour. The journal impact factor is just such a metric.

During a talk just over a decade ago, its co-creator, Eugene Garfield, compared his invention to nuclear energy. "I expected it to be used constructively while recognizing that in the wrong hands it might be abused," he said. "It did not occur to me that 'impact' would one day become so controversial."

As readers of *Nature* probably know, journal impact factors measure the average number of citations, per published article, for papers published over a two-year period. Journals do not calculate their impact factor directly — it is calculated and published by Thomson Reuters.

Publishers have long celebrated strong impact factors. It is, after all, one of the measures of their output's significance — as far as it goes.

But the impact factor is crude and also misleading. It effectively undervalues papers in disciplines that are slow-burning or have lower characteristic citation rates. Being an arithmetic mean, it gives disproportionate significance to a few very highly cited papers, and it falsely implies that papers with only a few citations are relatively unimportant.

These shortcomings are well known, but that has not prevented scientists, funders and universities from overly relying on impact factors, or publishers (*Nature*'s included, in the past) from excessively promoting them. As a result, researchers use the impact factor to help them decide which journals to submit to — to an extent that is undermining good science. The resulting pressures and disappointments are nothing but demoralizing, and in badly run labs can encourage sloppy research that, for example, fails to test assumptions thoroughly or to take all the data into account before submitting big claims.

The most pernicious aspect of this culture, as *Nature* has pointed out in the past, has been a practice of using journal impact factors as a basis for assessment of individual researchers' achievements. For example, when compiling a shortlist from several hundred job applicants, how easy it is to rule out anyone without a high-impact-factor journal in their CV.

How to militate against such a metrics-obsessed culture?

First, an approach that some have applied in the past and whose time has surely come. Applicants for any job, promotion or funding should be asked to include a short summary of what they consider their achievements to be, rather than just to list their publications. This may sound simplistic, but some who have tried it find that it properly focuses attention on the candidate rather than on journals.

Second, journals need to be more diverse in how they display their performance. Accordingly, *Nature* has updated its online journal metrics page to include an array of additional bibliometric data.

As a part of this update, for *Nature*, the Nature journals and *Scientific Reports*, we have calculated the two-year median — the median number of citations that articles published in 2013 and 2014 received in 2015. The median is not subject to distortion by outliers. (The two-year median is lower than the two-year impact factor: 24, down from 38, for *Nature*, for example.) For details, see go.nature.com/2arq7om.

Providing these extra metrics will not address the problem mentioned above of the diversity in citation characteristics between disciplines. Nor will it make much of a dent in impact-factor obsessions. But we hope that it will at least provide a better means of assessing our output, and put the impact factor in a better perspective.

However, whether you are assessing journals or researchers, nothing beats reading the papers and forming your own opinion. ■