The (blue) sky's the limit

Lunenfeld-Tanenbaum Research Institute's Jim Woodgett warns that neglecting basic research in favour of applied science is a mistake…

Modern societies invest in research for the compelling reason that history has repeatedly shown that it pays off with economic growth and prosperity. Societies without abundant natural resources, such as Japan, Taiwan and Singapore, have formalised investments in science and technology and protected these, even in times of economic and natural disaster. Emerging mega-economies such as India and China tend to plan for three or more times the rate of scientific investment than more mature economies.

Recognising its utter dependence on government support, scientific communities around the world have willingly promised their respective governments significant returns on investments in exchange for greater funding. For example, the $3bn cost of the Human Genome Sequencing Project has been claimed to generate economic returns in excess of 140 times the initial investment. It is hardly surprising, therefore, in a time of bloated budget deficits and high unemployment, that governments are looking to cash in on their investments and these previous promises. The obvious consequence is a shift towards more applied science, an increase in partnerships with industry and emphasis on lower risk development – leading (it is hoped) to new products and wealth creation.

There has also been a perceptible shift in the priorities of non-governmental agencies such as charities. In the health charity sector, there is increasing demand for donors to see the results that impact their loved ones sooner rather than later. Ever since US President Richard Nixon's declaration of a 'War on Cancer', hundreds of billions of dollars have been spent on research. There have been significant developments, better therapies and improved outcomes, but the number of people dying from cancer has hardly been affected, even when ageing demographics are taken into account. Donors, and by extension fundraisers, are right to demand better results. Surely, we know enough and it's only a matter of translating that knowledge into better drugs and treatments? The same is true for heart disease, diabetes, Alzheimer's, mental health, etc. Indeed, there are plenty of scientists and fundraisers willing to promise new cures in the foreseeable future.

These developments are all perfectly reasonable on the surface and, in times of fiscal pressure, entirely predictable. Governments and charities are in the business of improving the lives of their taxpayers and donors, not in keeping scientists employed. Why not accelerate the process, focus on products and generate new jobs, businesses and cures? Without new funding, such efforts necessarily redirect money previously targeted towards basic science, also referred to as 'blue sky' or 'discovery' science. Is this such a bad thing and, if so, why?

To answer this question first requires an admission of guilt by the research community. We have, either directly or by omission, given our benefactors the distinct impression that basic science behaves in a manner that is at least partially predictable. In other words, we have effectively bluffed what we do and how we operate, at least in terms as understood by our funders. The fact is that basic science cannot make reliable forward projections. There may be some exceptions, such as the Large Hadron Collider, which has provided such a technical advance in high-energy physics as to allow meaningful prediction of results, but in most cases, what we recognise as genuine breakthrough discoveries are largely serendipitous. That is not to say that basic science is random – clearly, there are environments and behaviours that favour success. The density of Nobel Laureates from the Laboratory of Molecular Biology in Cambridge defies the logic of pure chance in scientific impact. But it is also a truism that the most important work a scientist does is typically done before she/he is 40, at least in the life sciences. The reasons for this are complex, but also relate to reduction in risk and adaptation to mainstream dogma (not 'rocking the boat') that is a natural survival tendency in a world where research support is divided in three to five year increments with ever-decreasing chances of approval.

Indeed, the modern research machine is in danger of suffocating that upon which it depends most dearly: not funding, but originality of ideas. As funding has become tighter, funding agencies have demanded greater accountability and reporting. Peer review, the cornerstone of scientific adjudication that is meant to recognise the best quality ideas, has become cynical and conservative. Truly new ideas are typically shot down as being ridiculous or counterintuitive. We cling to our current models of the universe and only allow subtle, pedestrian refinements. Surely, the bulk of human knowledge cannot be wrong? Meanwhile, funding agencies, under direction from their masters, insert provisions and assessment criteria to encourage and reward characteristics such as 'relevance', 'impact' and 'socioeconomic benefit'. If we were being honest, basic scientists would point out that relevance is an incredibly poor predictor of original discovery. Major discoveries rarely have immediate use or benefit. They are often stumbled upon while asking completely distinct questions. Often, the significance is not fully appreciated by their discoverer, it is doubtful, for example, that Fire and Mello perceived the subsequent revolution in biomedicine enabled by their discovery of RNA silencing in the nematode worm (Nobel Prize in Physiology and Medicine, 2006).

The greatest threat to basic science is therefore not increased emphasis on translation or application of science. These are valuable and essential products of basic science, which feedback and provide future support. There has always been a broad spectrum of research, from the most basic of ideas to the most useful. What is far more dangerous is our arrogance and fundamental misunderstanding of the nature of ideas. That we generate more bioinformatics data each year than in all previous years combined reflects efficiencies in data generation, not understanding. The sheer volume of our knowledge base is not an indicator of its accuracy or utility. In other words, we have no idea how much more there is to be learned. All we can know is that it's immensely more than we currently perceive. As a single, obvious example, pharmaceutical development remains an impressively inefficient process where the vast majority of drugs fail at enormous cost. Is that due to big pharma incompetence (from each and every company) or the fact that our basic understanding of physiology remains woefully lacking?

In our race to squeeze faster fruits from science, we must be extraordinarily careful not to take shortcuts that asphyxiate our tenuous and ill-understood methods of birthing true discovery. We must avoid programming out the risk and initial absurdity that accompanies new ideas. We must be patient. We must, above all, stop expecting basic science to conform to our own inherently limited and established perceptions of the universe.

Jim Woodgett
Director of Research
Lunenfeld-Tanenbaum
Research Institute
Mount Sinai Hospital
Toronto
Woodgett@lunenfeld.ca
www.lunenfeld.ca