On research in a small country

Basic research and its practical applications • *by Michael Sela*

Let me say here that the minute a director of a first-class research institute begins to direct research in that institute, he should be fired. If he is allowed to do it, and the workers in that institute accept such direction, they should be fired, because you can take it from me, they are not worth the salt they eat. It's either one or the other—you just can't go fooling around with the independence of research workers.'

Thomas Milton Rivers, Vice President of the Rockefeller Institute from 1953–1955.

As humanity heads into the third millennium, the greatest impact—but also the greatest challenge—is the ever increasing amount of information and communication, particularly in the

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natural sciences. The progress here is truly enormous and it is sometimes running ahead of its legal, ethical and moral aspects. But as with all progress we must avoid an excess of information becoming a barrier to comprehension. In parallel, we must ensure that the work being done in research ultimately benefits humankind and human civilisation. For countries that invest in research and the development of new technologies, it is important to translate the accumulated knowledge into benefits for their population in order to justify those investments to the taxpayer.

Israel is a small country. Its population of 5.8 million and its gross domestic product of US\$ 105 billion are dwarfed in comparison with large countries such as the USA, Japan, France, Germany and the UK. However, it has managed to establish an excellent scientific base that makes it an important exporter of high technologies, most notably software and biotechnology. Israel has succeeded in

doing so because of the way it has been concentrating resources in science and technology on basic research as well as its application in order to strengthen its economic base. As a former president of the Weizmann Institute, Israel's leading research facility, I will lay out my ideas of how even a small country can excel in science and technology. I always see the contribution of the Weizmann Institute as not only improving the quality of life and the cultural and ethical values of our country, but also helping our economy either directly through the fruits of our research or indirectly as the ultimate source of scientific and technological manpower.

For a small country, the challenge is that we cannot be excellent in everything. But we have no right to make compromises in our effort to strive for excellence. Such a vision includes virtually complete academic freedom and the gathering of first-rate minds, which are then left alone to ripen at will. It also includes the free, frequent and informal exchange between men and women of various scientific disciplines from all over the world.

There is a fascinating dichotomy concerning the economic advantage of research for a country and its citizens. On a 'macro' level, it is obvious that the well-

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being of a country crucially depends on the level of science and technology developed there. At the 'micro' level of an individual scientist, however, it is difficult to perceive the 'greater good' and often the results are unrewarding. The great German physicist and physiologist Hermann Ludwig Ferdinand von Helmholtz put it this way: 'Whoever, in the pursuit of science, seeks after practical utility, may generally rest assured that he will seek in vain. All that science can achieve is a perfect knowledge and a perfect

understanding of the action of natural and moral forces [...]. Let each of us think of himself, not as man seeking to gratify his own thirst for knowledge, or to promote his own private advantage, or to shine by his own abilities, but rather as a fellow-labourer in one great common work bearing upon the highest interest of humanity.' In the same vein, Albert von Szent-Gyorgi, the Nobel-prize winning biochemist, said, 'discovery is seeing what everybody else has seen, and thinking what nobody else has thought.' Indeed, we must remember that there will be no applied science if there is no science to apply.

In many European countries, science policy is regarded as public support for the development of new technologies and their application in order to strengthen the country's economic base. Politicians often make a distinction between 'pure' basic science and applied research. I intensely dislike the notion of pure and applied research. If one speaks of pure research, one implies that the other is impure. I also prefer to talk about applicable research rather than applied research, because so little of what is applicable ends up being applied. At the Weizmann Institute, our philosophy is 'Research for its own sake', but whenever results from this free research have potential in the marketplace, we aim to pursue this energetically, preferably by our own industry. Let me show you an example of how our attitude of performing 'research for its own sake' can successfully contribute to the development of new products.

As a direct consequence of basic research on synthetic models of proteins, we developed a drug-vaccine against the exacerbating remitting type of multiple sclerosis. Although vaccines are well-established as the method of choice to fight infectious diseases, we are now extending this concept to include diseases of the autoimmune system: wherever it is possible to identify the putative cause of the disease, it should be possible to build a molecular analogue to combat it. When we found that

the positively charged protein of myelin sheath in the brain was capable of provoking an experimental disease in animals (allergic encephalomyelitis), we prepared an analogue of the peptide that would resemble the original protein in size, charge and

academic freedom is not freedom from budgetary constraints. In contrast to a university, which is supposed to teach every discipline, a research institute should concentrate only on those areas in which it can make a significant contribution.

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composition. We tried to induce the experimental disease with the synthetic polymer, denoted copolymer 1. Only when we had failed to induce the disease, did we try to use copolymer 1 in order to suppress the disease.

This positively charged polymer of four different amino acids has been approved as Copaxone in 20 countries, including the USA, Canada, Switzerland and the UK and has been successfully used by more than 40 000 patients. In the year 2000, sales amounted to around US\$ 250 million. Thus, a basic study led to a new and successful concept for the treatment of autoimmune diseases. Similarly, we prepared a peptide from Torpedo electric fish to treat myasthenia gravis, a muscle weakness due to auto-antibodies directed against the acetylcholine receptor. Our peptide successfully treats the experimental disease in mice and we are ready to start clinical studies soon.

Of course, a research institute such as the Weizmann Institute has several advantages compared to a university. The major difference is that the primary task of the university is the transmission of accumulated knowledge from one generation to the next, and its secondary task is to create new knowledge. For a research institute, it is entirely the opposite. But it is crucial to remember that a good university must also be excellent in research and that researchers at other institutions must also participate in teaching. Indeed, the presence of young scientists and doctoral students is the best defence a research institute has against calcification. Students should be encouraged to respect their older colleagues, but not to believe in everything they hear from them. Doubt is constructive and an important tool for successful research, as are optimism, perseverance and serendipity when luck meets the open mind. In this respect, the nurturing and encouragement of young scientists and an early opportunity to embark on their independent research careers are crucial, too.

Academic freedom is necessary for a productive research environment, but

And when money is scarce, there is a lot of wisdom in the approach that says: 'Strengthen what is the strongest.' Indeed, no institute can be the leader in every discipline. If there was a single managerial credo to which I stuck during my ten years as president of the Weizmann Institute of Science, it was that an administrator running a first-class institution must, however painful the procedure might be, draw up a list of priorities. Such immutable priorities must be defined with complete clarity and be unswervingly adhered to.

Although I have stressed the need for academic freedom, there is also, on the other hand, a definite need for co-ordination at the development level. The total scientific

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knowledge and the availability of scientific manpower should be assessed and co-ordinated at the national as well as the institutional level. However, we should refrain from introducing organisational changes too often, as the Roman general Gaius Petronius reminds us: 'We trained hard, but it seemed that every time we were beginning to form up into teams, we would be reorganised. I was to learn later in life that we tend to meet any new situation by reorganising, and a wonderful method it can be for creating the illusion of progress while producing confusion, inefficiency and demoralisation.'

Of course, in order to stay at the top, we must also make sure that the people whom we support do first-class work. Evaluation of scientists is always very difficult but it is an inevitable process to remain at the top of international research. From the very beginning, we used the method of peer review, consulting the best scientists in the world in a particular field on decisions of appointments and promotion. Publications in prestigious journals, as well as the extent to which those papers are cited are also good measures of quality.

Let me come to my last point, the philosophy of science, namely its international aspects. There is no endeavour more international than science and the community of scientists: individual long- and short-term visits, collaborations across borders, co-operation between universities and research institutes, national associations, and international unions. In my capacity as chairman of the European Molecular Biology Organisation Council for 6 years and having been involved in the establishment of the European Molecular Biology Laboratory in Heidelberg, Germany, I can only stress the enormous success and importance of this international research undertaking. Similarly, the establishment of the Asian-Pacific International Molecular Biology Network is another important step towards guaranteeing true international co-operation of scientists from all over the world.

I cannot tell other countries how to run science; I can only draw from my own experience. Every country eventually has to find its own ways to ensure that scientific research flourishes and benefits its population and economy. But no matter

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