CHAPTER FOUR

Scientific Research in a Free Society: Some Reflections

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INTRODUCTION

Scientific research is a diverse enterprise involving investigation into areas ranging from cosmology to methods for making better test strips to check blood sugars in people with diabetes. Between the arcane and the mundane there is a continuum of innumerable subjects. Given the varied disciplines covered and the disparate implications of research in these areas for society, it isn't possible to provide one answer to the appropriateness and role of research in a free society.

Of course, a strict anarchist-libertarian would have a simple and ready answer which would be "no." Since taxation is force and theft is inappropriate, the state has no right to steal, even for a goal such as understanding and curing cancer, let alone determining the nature of the universe. Whatever the force of these arguments, we live in society governed by a state, and that state is not going to disappear tomorrow or even in the next century. This state funds research under a number of programs. Since libertarians would like to see the state evolve in the direction of more rather than less freedom, it is reasonable to ask whether or not the state has any role in a free society and, furthermore, to examine the potential effects of participation of the state in research on overall freedom. Does state involvement in research lead to more or less freedom, or is it without any particular effect? If the overall effect is neutral, is there any justification for government-funded research?

In considering these questions I define research as inquiry into either biological, i.e., life sciences, and physical sciences. I specifically exclude research in such areas as economics and sociology, as their nature is intrinsically different from that of biological and physical science and they are also beyond my expertise. When giving examples I largely emphasize the life sciences, as my vantage point is that of a biomedical researcher.

BACKGROUND

"Life sciences" is a very general term covering a broad range of inquiry from basic biology, to biomedical science, to clinically oriented medical studies. Research in the life sciences includes basic research, applied research, and development. These represent a continuum of inquiry that ranges from pure knowledge-seeking as an end in itself to the development of products (pharmaceuticals or medical treatments) intended to cure human illness or create improved agricultural products. The extremes are easy to differentiate, but at the borders the basic research may be difficult to distinguish from applied research.

Basic research in the life sciences might involve research in cellular development in flatworms or molecules synthesized by fungi. Applied research might involve regeneration of neurons or adaptation of fungal products to inhibiting cholesterol synthesis. At the development end, the research would involve identification of drugs that stimulate neuronal growth or drugs that reduce cholesterol in people, and the effect of those drugs on incidence of heart attacks and strokes. Areas of zoology, botany, or yeast biology might be viewed as purely basic, without implication for human disease, however there are unexpected spillovers. For example, a hormone important for regulating pigmentation of fish skin is an important regulator of eating in mice and man. When one then considers the areas of microbiology or immunology, or genetics or behavioral neuroscience, the distinction between biology and biomedical research becomes increasingly difficult. Even when the test subjects are bacteria or mice the implications for medical research may be significant. Similarly, research performed on human subjects can have significant implication for basic areas. Human Immunodeficiency Virus was discovered in people suffering from Acquired Immune Deficiency Syndrome; however, studies of the HIV as virus as opposed to a human pathogen are more in the realm of basic virology.

The range from basic research to applied research and development is best seen as a continuum with fuzzy borders. In the area of neuronal degeneration, basic research might involve genes that regulate development of cells flatworms; translating this research to understanding genes that regulate development of neurons in mice is still basic, but as the implications of this reasoning to Parkinson's disease or Alzheimer's disease are possible to visualize, it borders on applied research. Looking for factors that might stimulate neurons to grow in culture or in mice is even more applied. Looking for factors that can be used as drugs because they exert their effects without toxicity is applied research but also has aspects of drug development. Finally, the clinical studies performed to see if the drugs work as expected in humans are entirely part of the drug development process.

In the United States life science research occurs at a variety of sites, including academic centers, pharmaceutical and biotechnology companies, independent research institutes, and a variety of government sites. Most of the research performed at academic institutions is in universities with graduate programs or medical schools. Colleges without graduate faculty may have small research programs, but these programs represent a minority of overall life science research. Independent research institutes are usually privately funded institutions with or without university affiliations. From the standpoint of performing life science research they function much like departments in universities; senior scientists have advanced degrees and credentials similar to university faculty, the laboratories may train post-doctoral fellows and (if the institute has a university affiliation) graduate students as well. For both pharmaceutical and biotechnology companies life science research is essential to maintaining drug pipelines and pushing drug candidate molecules through the drug development process.

At the government level, life science research performance sites are almost always federal facilities and include the National Institutes of Health (NIH), the Center for Disease Control (CDC), and medical departments of some of the Veterans Administration Hospitals.

FUNDING

In 1998 all research and development expenditures in the United States were calculated at $227 billion, representing a record level of funding. Of these dollars 66 percent were provided by industry and 29.5 percent by various agencies of the federal government; 2.2 percent of the budget came from universities and colleges (this includes state funding to state universities) and 2.5 percent of the funds were derived from other sources, including state government and local governments and nonprofit institutions. This current distribution of funding has evolved over a five-decade period since the World War II, during which the federal contribution first increased sharply from 20 percent to 62 percent in the fifties and sixties and then declined to its current levels. In the decade preceding 1998, the contribution of the federal government fell in terms of constant dollars as well. Contributions from all other sources fell as the federal share fell, and have risen correspondingly.[1] Hence, while all categories (basic, applied research, and development) are at currently historically high levels of funding, the growth has occurred in the private sector, in the face of declining federal contributions, indeed the federal contribution to industrial research and development; in 1997 federal funds represented 14 percent of total financing (an unprecedented low).[2]

The decline in the proportion of federal funding to overall research was also seen for funding of academic research. The federal effort peaked at about 75 percent in the late sixties and then declined to 60 percent in the late 1980s. It has remained stable since. In 1998 a total of $26.3 million (about 10 percent of total research and development dollars) was spent for research and development at academic institutions. Of this 59 percent came from the federal government, 19 percent from academic institutions, 8 percent from state and local govern-

1. National Science Board, "Science and Technology in Times of Transition," chap. 1 in *Science and Engineering Indicators—2000* (Arlington, Va.: National Science Foundation, 2000), fig. 1-1 and table 1-3. *www.nsf.gov/sbe/srs.*

2. National Science Board, "U.S. and International Research and Development: Funds and Alliances," chap. 4 in *Science and Engineering Indicators—1998* (Arlington, Va.: National Science Foundation, 1998), fig. 4-5. *http://www.nsf.gov/sbe/srs/seind98/start.htm.*

ments, 7 percent from industry, and 7 percent from all other sources. This distribution varies between private and public academic institutions. Private institutions receive 72 percent of their research budget from the federal government, only 2 percent from state and local governments, and 10 percent from institutional funds. The balance is supplied from industry and from nonprofit research foundations. Eighty-three percent of the total federal funding derived from three agencies: the National Institutes of Health (NIH, 58 percent), the National Science Foundation (NSF, 15 percent), and the Department of Defense (DOD, 10 percent). Other federal support came from the National Aeronautics and Space Administration, the Department of Energy, and the Department of Agriculture. During the past decade the proportion of NIH, NSF, and NASA funding has grown, while funding from the DOD, DOE, and USDA declined. In the life sciences (excluding psychology) virtually all federal funding comes from the NIH (89 percent).

Life science research dominates academic research in terms of both funding and distribution of research space. In 1997 expenditures in medical and life sciences totaled $8 billion, compared to $3.4 billion in engineering, $2 billion in physical sciences, $1.4 billion in environmental sciences, and $1 billion in social sciences. Similarly, biological and medical sciences utilized 40 percent of research space, compared to 15 percent by engineering and 14 percent by physical sciences.

SUMMARY OF BACKGROUND

The contribution of the federal government is not static, but continues to play a role in research and development in the United States. Funding has declined over the past four decades and now represents less than 30 percent of total research and development funding in the United States. Although the proportion of research funding to academic institutions has declined from absolute peaks in the late sixties, the total has declined. Most of the decline is in federal contribution to industry. Federal support to academic research has also declined but federal support still dominates support to academic institutions.

GOVERNMENT AND RESEARCH FUNDING

To look at the specific question of the potential role of government in research in a free society, let me first consider the role of government. Approached from an anarcho-capitalist perspective the government has no role. Society should be structured so that individuals choose their protective agencies to provide necessary services. There is no government to perpetrate a drug war; there is also no government to provide defense against enemy nations. In an anarcho-capitalist society the answer regarding the role of government in research is simple. There is none; hence if libertarians are simply anarcho-capitalists, they have their answer.

However, between a society structured along the protective societies of anarcho-capitalists and the current representative, quasi-paternalistic, partially redistributive democracy that is the United States government there is a continuum. This includes the minimalist state that Nozick argues protective agencies would necessarily evolve into,[3] and the Jeffersonian government-that-governs-best governs-least state that the founders had in mind. Just as Catholicism is only one Christian dogma, anarcho-capitalism is only one libertarian theory. Clearly individuals may be considered libertarians and still favor a minimalist state or a Jeffersonian state. It is possible that some libertarians simply would like to see the state eschew

3. R. Nozick, *Anarchy, State, and Utopia* (New York: Basic Books, 1974), chap. 2.

prosecution of victimless crimes, permit any and all behavior among consenting adults, and cease redistribution of wealth among individuals.

What might such a state look like? In the minimalist format, the state would provide police and national defense services and support a judiciary. It would be in the business of protecting the life and property of its citizens against force and fraud. These services might be financed through a flat tax that had a constitutionally defined maximum to prevent the finances of the state from becoming too robust, thereby providing a system of checks on government activity based on financial limits. There are many things that the state would not do; in fact, it wouldn't do most of the things associated with the modern state. The state would not: be involved in the activity of proscribing any behaviors between consenting adults, regulate trade, banking, or stock trades, provide senior citizens payments for health care, accredit medical schools, proclaim Secretaries Day or National Dairy Week.

Is there justification for such a state to be involved in any way in the pursuit of basic research or applied research or development? The answer depends on whether or not the state can fulfill its obligations to its citizens by relying solely on markets that have evolved privately. There are at least two areas in which it seems unlikely that traditional markets, uninfluenced by government, would be adequate for providing necessary products to the state. One is in the area of national defense and the other is in the area of public health.

The necessary involvement of the state in at least assessing and possibly subsidizing research at all levels in the area of defense seems obvious. Customers in the market for national defense products are competing nation-states. Common sense dictates that they will develop and jealously guard from their enemies both offensive and defensive weapons. Ideally the minimalist state will be interested only in the best defensive weapons, and it is unlikely that such weapons will be available from suppliers in other competing nation-states in an open market. Some technology might be shared with allies; however, the acquisition of forefront technology requires internal research and development. It's easier to control what is internally developed. It seems likely, in order to maintain a competitive position in defending its citizens, that the minimalist state would be required both to assess and invest in the engineering and science research involved in the manufacture of defensive weapons.

The necessary interest of the minimalist state in the areas of public health research and environmental research is less obvious. These sciences have been, to a significant degree, coopted by the political left and used as a rationale for proposing increasing state regulation, for anything from saving endangered snails to taxing high-fat foods to decrease rates of obesity in the adult U.S. population. While the politicization of these areas makes it difficult to objectively assess the significance of the claims and findings by scientists, nevertheless both public health issues and environmental issues can have direct effects on a populace.

It is completely consistent with libertarianism to claim that an individual's right to life entails a right to clean air that has an adequate oxygen supply. The extent to which human activities affect air quality should be of concern to a libertarian polity. If pollution leads to significant bodily harm, it follows that whatever agency provides protection for rights would have an interest in preventing the harm or offering a mechanism for obtaining restitution. The concern needs to be rational, and it can only be rational if the actual hazards can be defined. We can't say that the air needs to be clean, we need to ask how clean. In addition to being unpleasant, common pollutants cause small but measurable increases in asthma, bronchitis, and cancer. People who choose to live in cities like New York accept the small increase in risk. Over the past three decades, in United States cities air quality has improved, while disease risk has been reduced by laws regulating automobile emission controls. (If you doubt the effects of emission control on urban air quality, I recommend spending a few days in Athens, Greece, a city with inadequate emission controls.)

Meanwhile some environmentalists argue that emissions must be reduced further. Is this goal rational? Should people in Manhattan expect lower air quality than those living in Vermont? Answers require a risk-benefit ratio that can only be evaluated in the presence of data. The nature of the pollutants needs to be definitively known, the risk of the pollutants to health must be understood, and the cost of reducing the pollutants must also be known. The inquiry addressing these questions involves both environmental sciences and epidemiology. Environmental research would address the source of pollutants and their distribution in the environment, and epidemiology would address the prevalence and incidence of disease caused by pollutants. An excellent example of the difficulty in evaluating the problem of environmental pollutants can be found in a series of articles examining the "Arsenic Controversy" recently published by the Cato Institute.[4] Even the minimalist state would have an interest in funding such research, if such research were not being done privately, because the information might be essential for protecting rights.

When it is directed to addressing infectious diseases, the area of public health research might also be of legitimate interest to government. Does the government have any legitimate in-

4. "Special Report: The Arsenic Controversy," *Regulation* 24 (fall 2001): 42–54.

terest in infectious epidemics? I'll take it as a given that the state has no legitimate interest in noninfectious epidemics such as obesity. Although more than 50 percent of Americans are obese, and although this obesity has significant health consequences, it remains an individual problem related to the abundance of fat-inducing foods and a genetic predisposition to obesity. In contrast, infectious agents target individuals all the time during the annual cold and flu season and garner scant attention. This is because a cold or flu causes some inconvenience, but rarely complications. Companies lament losses in productivity and parents lament the days that their children stay home from school. Most people take it for granted that they'll get a virus or two in the winter but hardly expect the government to do anything about it.

However, the infectious world harbors nastier agents than myriad rhinoviruses causing colds. It harbors drug-resistant tuberculosis and malaria, and highly contagious, lethal viruses such as Llasa Fever and Ebola. Because infectious illnesses threaten life, to what degree should citizens expect that the state would be interested in protecting them from this kind of threat? Is the control of infectious epidemics a legitimate goal of the state? Infectious epidemics aren't purely a private concern. To the degree that they are infectious and potentially lethal, society has an interest in trying to identify and control epidemics. If this is a legitimate goal, then the state needs to ensure that there is adequate knowledge about the infections that might cause such epidemics.

It is possible that information for both environmental and public health questions would come from privately funded sources. To the extent that they are concrete problems such as smog, and have health consequences that are not to difficult to identify, as in asthma, citizens may well decide to fund agencies privately out of concern for their own health. To the extent that the problems are obscure, not immediate, either in time or geography, it may be necessary to centrally fund research that will address the problems.

Furthermore, infectious agents, some of which pose serious intrinsic threats, can also be used as weapons. The recent public health chaos over the possible threat of anthrax as a bioterrorism agent serves to highlight the need for current information in formulating policy decisions. Thus far the Center for Disease Control has promoted conflicting policies with regard to prophylaxis of individuals potentially exposed to anthrax. However, in what might be considered the "molecular era" of medical research, little work has been done on anthrax over the past twenty years. Other than a poorly coordinated, federally funded effort at generating an anthrax vacine for military personnel, there have no notable attempts at developing new treatments. In effect, anthrax, which poses little natural threat, is an "orphan" disease. The fifteenth edition of *Harrison's Principles of Internal Medicine*[5] has two pages devoted to anthrax and sixty to Human Immunodeficiency Virus. Physicians, the CDC, local public health departments have little information to go on. Local public health departments are also ill-prepared. Neither the public nor private sector provided adequate preparation, and had there been a widespread release of anthrax, hospitals and medical personal would have been significantly challenged to provide adequate care to those infected. It is possible that, absent the events of September 11, neither the private firms nor the state had any motivation to research anthrax, as any long-range view that it might be used for bioterrorism was considered

5. *Harrison's Principles of Internal Medicine*, 15th ed. (New York: McGraw-Hill, 2001), 914–15 and 1852–1912.

remote. However the reasons for considering anthrax as a weapon were credible and anthrax and other bio-weapons represent an area where defense interests and public health interests become confluent.

For example, if antibiotic-resistant anthrax were used as a weapon, it might be possible to treat anthrax with antibodies that interfere with the action of anthrax toxins. No such antibodies are currently available. In such a scenario, anthrax vaccine might also be effective. Hence it seems appropriate for the state to fund research in the area to ensure that efficacious prophylaxis and treatment are readily available. This is a problematic conclusion as it is not clear that future efforts would be more efficient than initial efforts at obtaining vaccine for troops. Also, it is important to note that this conclusion is not as firm as the conclusion regarding the role of the state in supporting research in traditional defense. Health care-related research may be inhibited or prohibited by regulations of the Food and Drug Administration or other government agencies. To the extent that this is the case, it is important to address these impediments and remove them before concluding that the support must derive from the state.

SUMMARY

The minimalist state will need to fund research to the extent that citizens expect it to protect them. Given that the market for national defense items is likely to be limited to other competing nation-states, the federal government will have to fund research into appropriate products for its own use. In the case of environmental and contagious public health issues, some or all research may be privately funded and the appropriate role of the state may be to ensure that sufficient research is done.

BEYOND BASIC OBLIGATIONS

If it is acceptable for the minimalist state to fund research intrinsic to protective functions that the citizenry views as contractual obligations, provided that such research isn't going to be financed privately, is it ever acceptable or desirable for the state to fund research outside the market, beyond what it needs to do to adequately fulfill its mission? I don't think that this is a question with a simple "yes" or "no" answer. For a pure minimalist state, the answer would seem "no." If the sole function of the state is to protect citizens against external threats, why would the state need to fund research outside the areas described above?

However, the minimalist state is a theoretical construct. The United States isn't a minimalist state. Assuming a relatively stable world, I doubt that many people would predict that the United States will evolve rapidly into a libertarian minimalist state over a few decades. It's not practically possible to predict how the world or our nation will evolve over the next century. Most of the predictions made in 1900 were wrong, so it is worth asking the question about the appropriate role of the state in the context of present reality. Our state, a representative democracy that engages in some redistribution of wealth, exists in a world with other states, most of which are less democratic and engage in greater degrees of redistribution of wealth. In this context should the state support research? Should the support be limited to certain kinds of research? Is the support of research likely to increase or decrease personal freedom? It is beyond the scope of this essay to explore the nature of personal freedom, so I will be conventional and say that personal freedom is the ability of an individual to be a project-pursuer,[6] to act in a way that fulfills individual desires and goals as long as, in the process, one does not engage in force or fraud. Wealth typically correlates well with personal freedom in that the wealthy find it easier to pursue projects than the poor. Similarly, it is easier to be a project-pursuer in a wealthy society than in a poor one because wealthier societies are freer and less susceptible to tyranny. To the extent that discovery and invention have improved health and productivity, scientific research increases wealth. As economics is beyond my area of expertise, I refer the reader either to a serious libertarian approach to the subject or alternatively to P. J. O'Rourke.[7]

The United States spends more money, both private and public, in the pursuit of research and development than any other nation, and certainly produces the highest percentage of publications in every scientific field (although on a per capita basis Switzerland, Sweden, Israel, and Denmark are more productive).[8] In terms of a journal-impact factor, of the top five journals four are published in the United States (*Cell*, *New England Journal of Medicine*, *Science*, *Journal of Experimental Medicine*) and one is British (*Nature*). The combined dominance of the United States and Britain in science has led to an inexorable shift to English as the main language of science. As of 1997 95 percent of papers actually cited by another paper were published in English, compared to 83 percent in 1977.

The U.S. economy is the world's largest and citizens enjoy

6. L. Lomasky, *Persons, Rights and the Moral Community* (Oxford: Oxford University Press, 1986).

7. P. J. O'Rourke, *Eat the Rich* (New York: Atlantic Monthly Press, 1998).

8. T. J. Phelan, "Evaluation of Scientific Productivity," *Scientist* 14 (2000): 39.

one of the highest standards of living. To what degree is this success related to the success of technological industries? Causality seems hard to prove, but it is clear that both prosperity and productivity are associated with the high-technology products. Analysis of the global marketplace in technology indicates that the United State is the leading producer of high-technology products and is responsible for one third of these products. High-technology industries include computers, pharmaceuticals, communications equipment, and aerospace. During the 1990s, the United States has gained market share in all but the aerospace industry. Overall high-technology industries are important in the generation of wealth.[9]

Assuming that a specific activity does not result in decreased freedom and is not meant to substitute for activities already privately supported, it does not seem to me to be antithetical to libertarian principles to have the government support certain types of research if the intent of the activities is to increase knowledge, wealth, and, ultimately, freedom.

How might state funding of research *decrease* freedom? To consider this question we first need to examine the nature of research. Research is an activity performed by scientists, usually in a laboratory setting. The scientists are there voluntarily. If the research involves human subjects, an extraordinary number of precautions are taken to ensure that the subjects are also there voluntarily and have given informed consent. When the subjects are vertebrate animals, care is taken to ensure that the protocols used are appropriate and that the researchers minimize pain. If research is performed in an academic setting, the results of the research belong to the laboratory performing the

9. National Science Board, "Industry, Technology and the Global Marketplace," chap. 7 in *Science and Engineering Indicators—2000* (Arlington, Va.: National Science Foundation, 2000).

research. It is the responsibility of the lab chief to ensure that the data are reliable and to disseminate the results. In an academic setting, any potential patents name the investigator as inventor. Even if the government has funded the research through an agency such as the National Institutes of Health, it eschews ownership and allows the institution to own the patent. A significant portion of state-funded research (most of the portion not used to fund defense) is a voluntary activity engaged in by scientists at academic institutions. Although government-funded, the ethos of the research taking place at academic institutions comes from the academic environment. Funds are derived from the state, but participation as a scientist or as a subject is voluntary.

The possible concern for coercion is that state funding of research generally means that the funds come from taxpayers. A libertarian who feels that any payment of taxes is a coercive activity cannot possibly condone government funding of basic research. A libertarian who feels that some taxation is permissible (be it in the form of a flat tax), because of the benefits of living in a free and wealthy society, might be convinced to support basic research on the basis of future returns. The total contribution of the federal government to all research and development is $66.9 billion. This represents 4.0 percent of the $1.652 trillion federal outlays of 1998. The amount spent at academic institutions was 1.5 percent of the total budget.[10] Compare this to the total 35 percent of the budget spent on the largely unjustified transfer of wealth from younger individuals to older individuals in the form of Social Security and Medicare payments. A society that eschews enforced transfers

10. U.S. Census Bureau, *Statistical Abstract of the United States: 2000*, table 532.

of wealth can well afford to fund research on the income from a modest flat tax.

THE PROBLEMS WITH A MARKET FOR RESEARCH

Ideally, funding for research should come from private sources. For any particular area of inquiry, the nature of the research ranges through a continuum of basic to applied. The more basic the question, the lower the likelihood of private funding. Why? It is because the product of basic research is information, which only has market value if it can be sold or traded for something else. For example, the information "this is the gene that codes for erythropoietin (EPO), a hormone that stimulates red blood cell formation" has value because EPO can be sold (and indeed is now sold) to people who are anemic because of low EPO levels. The information "this is the gene that encodes for the hormone, melanin concentrating hormone (MCH), a hormone that causes fish color to lighten" has no economic value because there's no known market for treating fish with expensive peptides to change their skin color. Basic research is pursued with the sole intent of understanding a biological or chemical or physical process and without any specific intent to produce products. Although ultimately the research may have broad applied implications, these may have never been envisaged by the scientists making the original observations.

Let's consider the story of a well-known molecule, insulin. As potential users of medical care, most us living in Western democracies take for granted that if we develop diabetes and require insulin we will be able to go to the drug store and readily purchase insulin. Most of the potential users are unlikely to consider the source or the history of the product, which illustrates the interaction of basic and applied research and, I think, illustrates the problems of expecting market forces to fund basic research.

Insulin was discovered in early 1920s as part of an applied research effort. It was already known that removal of the pancreas in dogs led to a syndrome of high glucoses that looked similar to human juvenile diabetes. The effort, which was not the first to isolate insulin, was initiated by a surgeon, Frederic Best, who later (if somewhat controversially) won the Nobel Prize.[11] Insulin was first introduced as a life-saving drug isolated from either beef or pork pancreases in 1922. Insulin worked well enough, at least in juvenile diabetics. Eli Lilly and Company was the main manufacturer in the United States. Beef pancreases were more abundant but pig insulin, which differs from human insulin by only one amino acid, was considered a better product because it was less likely to produce allergic reactions. Between 1922 and the 1970s the major research efforts of Lilly and the European manufacturers of insulin (Novo and Nordisk) were aimed at refining the purification methods and the formulations to create short, intermediate-acting, and long-acting products. Insulin may have provided a large profit for these companies, yet none were involved in further studies aimed at understanding the molecule.

Still, insulin was the subject of basic research. In 1953 Fred Sanger reported the sequence of human insulin.[12] This was a historically important finding because what is now obvious, that specific proteins have specific structure of amino acids

11. M. Bliss, *The Discovery of Insulin* (Chicago: University of Chicago Press, 1984).

12. F. Sanger, "The Arrangement of Amino Acids in Proteins," *Advanced Protein Chemistry* 7 (1952): 1–67.

from end to end, was then a subject of debate.[13] In the 1960s, three groups, one in the United States, one in Europe, and one in China, reported on the chemical synthesis of insulin, demonstrating that this fairly long protein could be synthesized through a series of chemical reactions in a test tube. The chemical synthesis of insulin was a scientific climbing of Mount Everest and had about equal commercial use because the synthesis was too expensive to be considered by industry. For a brief period, in the mid-to-late 70s, physicians involved in the treatment of diabetes voiced concern that by the year 2000 there would be a global shortage of insulin. As the number of insulin-treated diabetics grew, it seemed unlikely that the material from slaughterhouses would be adequate to supply the demand.

Between the discovery of insulin and the synthesis of the peptide, other discoveries were made. The structure of DNA and the nature of the genetic code were discovered in 1952, followed by a couple of decades studying DNA and genes, mostly in one bacterium, E. coli, a resident of human gut. A lot of this work focused on subjects that seem arcane, even to me. How much do you want to know about mutations in DNA factors regulating production by bacteria of an enzyme that breaks down the sugar galactose? The research had no commercial applications and the scientists were unlikely to win public acclaim by discovering the cure for cancer. Even if you've studied biology in college you may not remember that Jacob and Monod won the Nobel Prize in 1965 for their discovery of the lac operon, a regulator of a bacterial gene.

Meanwhile, much information about bacteria was being discovered. Because of their nature, bacteria are susceptible to

13. J. Darnell, H. Lodish, and D. Baltimore, *Molecular Cell Biology* (New York: Scientific American Books, 1986).

invading bits of DNA, and to deal with foreign DNA make enzymes that degrade it. However, the bacteria have to distinguish between their own DNA and invading DNA. Bacteria accomplish this through molecules known as "restriction enzymes." The earliest reports on the enzymes, dating back to the late 1960s, were published without much fanfare. While the information might seem as arcane as the information on lac operon, these restriction enzymes form the basis of the biotechnology revolution.

Scientists, notably Arthur Kornberg, spent years studying the mechanisms by which DNA is synthesized and degraded, in the process discovering a number of enzymes that could be used to manipulate DNA. For example, scientists can ligate pieces of DNA cut with a restriction enzyme to other pieces of DNA or make copies of DNA that they already have. Using the variety of enzymes derived from examining bacteria, scientists can now identify a gene, make a probe to study it, modify it, devise a way of making the product of that gene, and ultimately engineer a bacterium or a yeast cell that incorporates the gene of interest in its genetic material and makes the product protein. Alternatively they can engineer a mouse that makes the peptide they are interested in, in the chosen tissues. Nature puts insulin production in the pancreas, but a scientist could place it in the stomach or in the testicle. If you're a scientist and you're feeling particularly silly, you can make a rabbit that glows green.

One of the first genes to be manipulated in this way was the insulin gene. In the mid-1970s a group of research scientists led by Walter Gilbert at Harvard Medical School described the identification of the gene for insulin and the production of insulin by a bacterial clone.[14] Within a few years scientists had

14. L. Villa-Komaroff, A. Efstratiadis, S. Broome, P. Lomedico, R.

generated recombinant bacteria capable of manufacturing insulin, and within a few more years part of the world's insulin supply was coming from large fermentors housing billions of bacteria busily making a human protein entirely foreign to the bacterial chromosome. Today the vast bulk of the world insulin supply is manufactured through the use of genetic engineering and what is sold at the drug store is "recombinant human insulin."

It is not surprising that once Gilbert isolated the gene for insulin, pharmaceutical companies would imagine how to exploit the discovery. However, the 1978 paper reporting on the synthesis of insulin by E. coli was based on almost three decades of research without commercial applicability. Kornberg has commented, "No industrial organization had, or ever would have, the resources or disposition to invest in such long-range, apparently impractical programs."[15]

Basic research, in its pure form—the investigation of processes aimed solely at understanding the process—is an activity that cannot be sustained by a market. The study of DNA replication in bacteria yielded interesting information on the nature of bacteria, but the interest was limited to a small audience, other scientists interested in DNA.

What's the market for the results of basic research that have no possible commercial information in the foreseeable future? It has enough value to be published in journals, but science journals do not pay royalties to the authors. Publication confers prestige, especially if other scientists like the work and cite

Tizard, S. P. Naber, W. L. Chick, and W. Gilber. "A Bacterial Clone Synthesizing Insulin," *Proceedings of the National Academy of Sciences USA* 75 (1978): 3727–21.

15. A. Kornberg, "Support for Basic Biomedical Research: How Scientific Breakthroughs Occur," *The Future of Biomedical Research*, ed. C. E. Barfield and B. L. R. Smith (Washington, D.C.: American Enterprise Institute and Brookings Institution, 1997).

it. But the prestige has a limited audience; it is other scientists that understand the work. Information that can't generate commercial interest is information that has no market value if you can't make a drug, build a faster computer or a more energy-efficient furnace.

Intrinsic to the nature of basic science is that it is pursued without any clear-cut awareness of the market value of the information. Scientists doing basic research today have motivations not dissimilar to scientists in the time of Aristotle. Aristotle considered nearly every aspect of the world that he observed[16] from the vantage point of a scientist, because it was there to be catalogued, not because of the marketing potential of what he had catalogued. Value, to a basic researcher, is a publication in *Nature*, *Cell*, or *Science*. A patent and royalties might be nice, as they might pay for the college education of the scientist's offspring, but they aren't the goal. Although many scientists dream occasionally about doing something worth a Nobel Prize, most work with enthusiasm knowing they are never going to win one. Not only are the products of basic research not subject to value in a conventional market, but those laboring at basic research tend to ignore the rewards of the conventional market. Many scientists working in an academic institution could easily increase salary by 50–100 percent working for a biotech or a pharmaceutical drug company, yet excellent scientists stay in academics, with lower salaries and the problem of worrying about grant funding in exchange of the freedom of pursuing basic questions.

Even if basic science produces products that are of questionable immediate market value, why not rely on concerned citizens funding basic research privately? Concerned citizens band together to form organizations that fund disease-related

16. Aristotle, *Selected Works*, trans. H. G. Apostle and L. P. Gerson, 3d ed. (Grinnell, Iowa: Peripatetic Press, 1991), 1–27.

research such as the American Diabetes Association, the American Heart Association, and the March of Dimes. Generally the total effort funded by these organizations is small, and although some basic studies are funded, much of the research is aimed at finding a cure. Private philanthropy aimed at funding basic research is unusual. The Howard Hughes Medical Institute is unique, both in its method of funding individuals rather than projects and in contributing to biomedical research. In 1993 it contributed $268 million to biomedical research. Although this contribution is significant, coming from a single organization, it represents only about 1 percent of total research funding. Would private agencies contribute more if the government contributed less? This seems unlikely, given the fact that this source of funds has been stable at 7 percent of academic research and development funding for over three decades.

Investment by biotechnology industry and pharmaceutical companies in research is significant, but it tends to be directed at research where at least a product can be envisioned. I referred to the gene for the fish hormone, MCH, as an example of a bit of information that has no commercial value. Indeed although the hormone was identified a British group in 1983, pharmaceutical companies had no interest in this substance until 1996 when my research group demonstrated that in mammals, MCH stimulated feeding behavior. Going from a fish hormone mediating color change to a mammalian neuropeptide important in appetite and obesity changed the interest of industry, and I am now aware of a number of companies with MCH projects. However, in 1983 no company could have convinced investors that MCH was a project worth working on.

Investment by private individuals in basic research without a disease focus through charitable organizations is unlikely to happen. As discussed above, the benefits of basic research may only be seen long-term. Most individuals don't have enough understanding of scientific process to grasp the long-term consequences of basic research. It is depressing to note that only 11 percent of Americans can define the term "molecule" and only one in five can provide a minimally acceptable definition of DNA. Only 50 percent reject the statement that "the earliest humans lived at the same time as the dinosaurs." Astoundingly only 48 percent know that the earth goes around the sun once a year![17]

Finally, with regard to government funding of basic research, I believe that funds should be directed to universities and institutes outside the federal government. The National Institutes of Health supports some intramural research of generally high quality. However, there is nothing special this research. As the subject areas explored at the NIH are explored elsewhere, there seems to me no justification for directing government funding at government institutions. A notable exception may be the Center for Disease Control, particularly in its role in identifying and monitoring infectious epidemics. This public health role may be hard to duplicate in a private setting.

SUMMARY

The products of basic research do not necessarily have market value and the individuals that pursue basic research do not necessarily act to maximize their own economic circumstances. The results of basic research may have long-term market value, however. Private investment is usually directed at

17. National Science Board, "Science and Technology: Public Attitudes and Public Understanding," chap. 7 in *Science and Engineering Indicators—1998* (Arlington, Va.: National Science Foundation, 1998). *http://www.nsf.gov/sbe/srs/seind98/c7/c7s2.htm.*

knowledge that has short-term value. Neither industry nor private charity has a record of funding research for the sake of research. Funding as a potential government activity is reasonable if it is aimed at activities for which the government has obligation to citizens (such as defense). Funding is also permissible if it is directed at research that would not be supported by market forces and if it is aimed at increasing freedom and wealth.

THE DOWNSIDE

Assuming that one agrees that in a free society it is reasonable for the government to fund basic research in the life sciences and the physical sciences, with the constraint that this research would not be otherwise funded, the potential negative consequences of actually enabling funding need to be considered.

One negative is that a certain amount of money would be wasted. This seems to be a given in any human activity. Even pharmaceutical companies, where there is constant pressure to create products and watch a bottom line, fund projects that never yield results. The extent to which money is wasted will depend both on the total funds available and the level of funding, and on the mechanisms by which the funding is distributed. An analysis of the NIH review process, which funds "projects," is beyond the scope of this chapter. However, it is important to note that at present 25–30 percent of investigator-initiated grant proposals are funded after a peer-review process. The process is not perfect, however the process is competitive and there is a serious attempt to fund the best science.

Another negative is that science will be politicized. This certainly happens. Jerome Groopman has written an excellent article on history of the war on cancer.[18] When Richard Nixon

18. J. Groopman, "Annals of Medicine: The Thirty Years' War: Is There a Better Way to Fight Cancer?" *New Yorker*, June 4, 2001.

declared a war on cancer in 1971, he was responding to lobbying efforts by the philanthropist Mary Lasker and the pediatric oncologist Sidney Farber. As Groopman points out, the war has not been won, despite significant funding. The initiatives were criticized at the time by a number of scientists who felt that a cure would not come by directive. Dr. Francis Moore, a medical historian, referred to the "law of unintended consequences in scientific discovery." Much of discovery happens by chance, which is the point of funding basic research in the first place. Dr. Moore pointed out that anyone interested in scientific discovery would not have supported the work of John Enders when he attempted to grow mumps virus. No one would have predicted that this work would lead to the process that produced polio vaccine. Yet we see examples of politicized funding frequently. The efforts directed at increasing breast cancer and HIV funding for finding cures are political efforts by interest groups. Scientifically there is no reason to expect that major advances in these diseases will necessarily come from directed research efforts as opposed to a serendipitous discovery made by a scientist examining an unrelated process.

Other types of political pressure also emerge. Special efforts are aimed at increasing the rates of participation of underrepresented minorities in research, however private initiatives are hardly immune to this pressure. In 1994 the Hughes Institute made serious attempts to increase the participation of women and minority groups in its research programs.[19]

There is also the potential of funding fads. A recent NIH initiative involves funding of research directed at alternative therapies, which might be useful to the extent that rigorous clinical studies are aimed at examining real effects of alternative therapies. The purveyors of alternative therapies seem to

19. K. Y. Kreeger, "Hughes Institute Moves to Bolster Female and Minority Participation," *Scientist* 8, no. 7 (April 4, 1994): 1.

be either unable or uninterested in performing such studies. If the money is used by alternative therapists to show borderline psychological benefit of such therapies, it is likely that the money will have been wasted.

Finally, a significant risk of permitting government involvement in research is that there are and will continue to be attempts by institutions and individuals to acquire support outside the peer-reviewed funding process. It is well known that line items can be added to appropriations budgets to fund congressmen's pet projects. Such funding, which is hard to identify, has been used to fund research projects at medical centers and universities. It is difficult to see this as anything other than pork-barreling, which I believe is antithetical to the aims of a free society.

These potential problems indicate that the process of funding needs frequent review and that its necessity cannot be assumed. The proportional contribution of federal funding to research has declined since the peaks of the 1950s and 1960s, and we can't assume that some level will always be needed. Depending on the nature of discovery, the need for funding may decline as more processes are understood. Alternatively, areas of current questions in basic research may open other areas, so the need for basic research may be necessary for a long time to come.