ASSESSING THE PROGRESS OF THE GENETICS REVOLUTION

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The industrial revolution in applied genetics dates back to 1973 with the discovery of plasmid-mediated gene transfer, more commonly known as recombinant DNA. Within a few years, there was a rapid growth in the formation of new biotechnology firms (NBFs). The firms were positioned in a number of sectors including industrial microbiology, chemical, energy, mining, food processing, cosmetics, pharmaceuticals, medical diagnostics, agriculture, and livestock. The extent to which so many industrial sectors responded to the innovations in applied genetics signalled the breadth of the genetics revolution. The growth of new biotechnology firms peaked between 1980 and 1982 and then began to decline. Established corporations invested heavily in research and product development beginning in the early 1980's. For example, in 1982 biotechnology represented 28%, 22%, and 47% of the R&D budgets of Monsanto, Eli Lilly, and Schering Plough respectively.

Investments in biotechnology have been greatest in the areas of pharmaceuticals, diagnostics, and agriculture. The first generation of products has also appeared in these sectors.

With more than a dozen years since the birth of modern biotechnology, how can we assess the progress of this industrial revolution? This is no simple task. One has to identify criteria and establish a vantage point from which to discuss the assets, liabilities, realized and unrealized expectations, successes, and failures of the new genetic technologies. A one-sided approach to assessing the progress in biotechnology is to look exclusively at financially "successful" outcomes. It is a mistake to define progress exclusively in market terms of "successful" products and processes without evaluating how they contribute to the reservoir of human knowledge, the quality of life, whether they meet human needs and enhance the quality of the environment, and how they compare to the technologies or products they replace, i. e., what is gained and what is lost.

The notion of success in industrial development is a relational concept. One has to speak of success to someone: to those involved in the development; to investors, to scientists; to other sectors in the economy; to the general public. Progress in biotechnology may be viewed differently depending on the criteria used and the vantage point of the evaluator. Even at this nascent state in its development, biotechnology is too complex a phenomenon about which to give a simple progress report. Have there been dramatic developments? Without a doubt. Has biotechnology lived up to its promises? Only somewhat. Are all of its outcomes and its expectations unambiguously positive? Not by a long shot.

Scope of an Industrial Revolution

Technological innovations may be measured by the depth and breadth of their penetration into the industrial economy. The depth of penetration is determined by how great a transformation is made within a single sector. Thus, if advances in photovoltaic technology were to result in solar cells that generate 50% of domestic electricity, this advance would be considered "deep" revolution in energy production.

The breadth of a technological revolution is determined by how many sectors of the economy are affected. The discovery of electricity and development plastics represent technologies of considerable breadth since the impacts were felt throughout many sectors of the industrial and domestic economy.

Simply on the criteria of sector impacts, biotechnology qualifies as a technological revolution of considerable breadth. The number of by-products and applications covers many sectors of the economy even at this early stage of its development.

The depth of its penetration has already been demonstrated in the pharmaceutical and medical diagnostic sectors. The techniques of monoclonal antibodies and recombinant DNA research have made it possible to develop totally new pharmaceuticals and to revolutionize the manufacture of existing pharmaceuticals. In theory, vaccines can be made safer and more efficiently using gene splicing. The reason for this is that a single stable protein on the outer coat of the infectious virus may be cloned and used as the immunizing agent, eliminating the need for working with the whole intact virus.

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Economic Success

A widely used measure of success is given in terms of economic value added. What is biotechnology's contribution to the economy? A 1988 study of the Office of Technology Assessment estimated an annual U.S. investment in biotechnology from all sources (Federal Government, states, and the private sector) to be between $4.3 - 4.9 billion. A small percentage of this investment has resulted in successful products. In 1980 not a single company made any earnings by manufacturing and selling a product developed through the new generation of bioprocess technologies. In 1984 OTA reported that even the most mature NBFs have only a few products to generate revenues that may be used to cover operating expenses. Most firms were still dependent on research contracts for revenues. By 1988, it was still the case that no biotechnology company was able to report a profit solely from the sale of a product, but the number of products submitted for review to the Food and Drug Administration and to the Environmental Protection Agency rose significantly.

Another indicator of economic growth of the industry is the growth of public stock offerings. Between 1982 and 1983 public stock offerings grew from approximately $180 million to nearly $600 million. More recently the stock market has been fickle to biotechnology. In 1988 the overall industry was still losing money. However, these economic indicators tell us little about the contributions that biotechnology has made or promises to make to the quality of life. It is, therefore, a narrow lens with which to judge process.

Meeting Expectations for Biotechnology

Has the biotechnology revolution met its early expectations? We can respond to this question by selecting three widely publicized medical and pharmaceutical products: human insulin, human growth hormone, and interferon, as well as a few generic ideas in agricultural applications—biopesticides, nitrogen fixing plants, and herbicide resistant plants—and evaluating their progress to date.

Human insulin was developed for the first time by genetic engineering techniques. It was the first drug manufactured by those techniques to be approved for human use. It is therefore a product whose existence is a direct outcome of rDNA. For many diabetics it is at least as effective as the bovine and porcine insulins — that is with regard to potency and antigenic activity — and much "cleaner" to manufacture. Eventually, it may displace the animal insulins, but physicians are not automatically switching patients who have done well on animal insulins. It is worth noting that the price of human insulin has not been revolutionized and runs 20-30% higher than the bovine-porcine insulins but is comparable or somewhat lower in price than the pure porcine insulin. Nevertheless, the microbial production of human insulin serves as a model for the manufacture of a vast domain of human proteins. In that sense its expectation has been met.

Human growth hormone (HGH) was the second drug approved for use by FDA in 1985. Prior to recombinant DNA, HGH was produced in limited quantities from the pituitary glands of cadavers. The benefit of rDNA-manufactured HGH was widely acclaimed upon discovery that the HGH obtained from human tissue was sometimes contaminated with a pernicious virus that causes Creutzfeldt-Jacob disease. The genetically engineered product, which was free from viral contamination, soon replaced the traditional method of harvesting cadavers. Initially it was sold at a price below that of pituitary-derived growth hormone although the cost of a year's treatment (ranging from $8,000 - $16,000) still remains substantial and requires federal subsidy.

Thus far, the manufacture of microbially-derived HGH has been proven successful for those people who are afflicted with pituitary dwarfism. Questions have been raised about other possible uses of HGH including treatment of normal but short-statured people and its use for those who wish to build muscle tissue. Little is known about the long-term effects of such uses. But since pituitary dwarfism does not represent mass markets for HGH, the value of the hormone for wider uses remains questionable.

Of the first generation pharmaceuticals pursued by the new biotechnology industry, interferon was among the most publicized. The media spoke of it as a natural virus fighter with potential to prevent or cure the common cold, hepatitis, cancer, and even AIDS. Gene splicing has made it possible to produce large quantities of several varieties of human interferon. It has contributed to a substantial amount of research and stimulated the development of a cottage industry that has formed around the promise of this drug. However, the expectation that interferon might do for viruses what antibiotics has done for bacteria has thus far not been realized.

Biological Pesticides

Much has been said about the potential in biotechnology for weaning the agricultural sector from its dependency on chemical pesticides and replacing it with environmentally safe biological pesticides. This is still an unfulfilled promise, but one in which both the rhetoric and the investments have expanded dramatically in the past few years. Environmentalists will consider this development in biotechnology successful when it creates a more natural and balanced approach to agriculture. Those who work or invest in biotechnology may view success in terms of expanding markets. Thus, a herbicide resistant crop which is compatible with and supportive of chemical insecticides may be viewed as a success by some members of society, but will be viewed as an assault on the environment by many others.

Ice minus was the first rDNA-produced biological pesticide approved for field tests. Assuming it is completely safe in the environment, it may benefit farmers by reducing frost damage to crops during periodic cold spells. The success of this product has to be weighed against existing methods for reducing frost damage. Currently, these methods do not include the use of insecticides. The product has been met with some skepticism on the part of farmers who have already invested capital into frost-protecting technologies and face the prospect of surplus crops, low market prices, and increased acreage devoted to agriculture. Thus, while a company has announced the technical success of ice minus in a laboratory and field studies, it is still premature to evaluate its total impact on the agricultural system.

Another widely discussed biopesticide is either a plant or a natural organism into which has been introduced a toxin gene from *Bacillus thuriengienses* (Bt). The toxin in question is lethal to certain pests that feed off food crops. Should a safe product emerge, it would be a clear example of how biotechnology might replace broad spectrum chemical insecticides with natural toxins that are species specific. Once again, it is too early to tell how this promise of the biotechnology revolution will fare. But its pursuit follows a venerable tradition that dates back at least to the publication of Rachel Carson's *Silent Spring*.

The massive use of synthetic fertilizers in agriculture has had a toll on the environment. Nitrogenous and phosphoric compounds have run off the land, contaminated lakes and contributed to their eutrophication. Two contributions to solving this problem have been associated with biotechnology. First, there is the possibility of enhancing the natural nitrogen fixing capacity of microorganisms that live around the roots of plants. Second, there is a research strategy to incorporate the nitrogen fixing genes directly into the plant. These programs have not yet achieved a level of success that would elevate biotechnology in the minds of environmentalists. Progress has been incremental and less than dramatic compared to pharmaceutical and diagnostics.

Conclusion

For the biotechnology industry to get off the ground, it had to be sold aggressively first to venture capitalists and then to established companies. The industry carried a great burden of expectations. In its first dozen years, a few of the expectations have been realized, particularly in areas of health care. Most of the other expectations in agriculture and renewable energy sources are still far from realization.

Some of the applications of biotechnology in the food industry will be viewed very favorably by the processed food sector. For example, the use of gene splicing methods to produce fructose can reduce costs of sweeteners in food processing. Or microbially produced cocoa may shift the dependency of U.S. candy manufacturers away from foreign suppliers. From a global perspective, the countries that depend on cocoa as a major export crop can face major economic destabilization. Barring a radical shift in price for consumer goods, the American public will, for the most part, be unaware of and unaffected by the shifts in product inputs. This is also true for much of the chemical manufacturing industry if microorganisms are substituted for pure chemical processes.

From a global public interest perspective, the most important areas for biotechnology to pursue are the production of vaccines for major world diseases, such as malaria and AIDS; the development of treatments for heart disease (e.g, clot-busting drugs and early warning diagnostics) and cancer; the reduction of chemicalization of agriculture while maintaining crop yields, and the providing of opportunities to Third World nations to develop their own renewable resources and health care products. These, and not the arcane applications to cosmetics and transmogrified animals will enhance biotechnology's image as a technological revolution that contributes to the progress of civilization.

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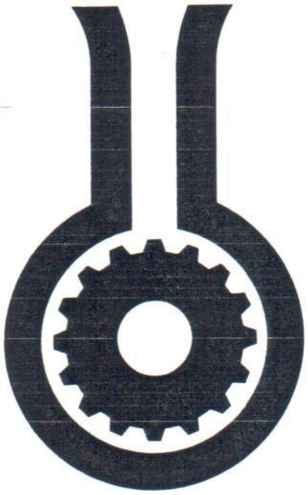

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