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The Potential Spinoff of Advances in Human Medicine to Animal Research and Agriculture

BIOTECHNOLOGY AS A GROWTH INDUSTRY

The discoveries of biotechnology will soon be approaching 20 years of age. Several of the key discoveries—restriction enzymes (Kelly and Smith, 1970), DNA ligases (Weiss et al., 1968), etc. led to the first transformed microbe in 1973 (Cohen et al., 1973). These initial discoveries led to an extended discussion, in 1976, in a San Francisco tavern between a venture capitalist Robert A. Swanson and Herbert W. Boyer of the University of California in San Francisco. The first biotechnology-based "boutique," Genentech, was thus soon formed. Genentech's success led the way to the creation of hundreds of other small companies specializing in applications of an emerging technology—genetic engineering. The excitement, dreams and speculation generated by this technology attracted billions of dollars of venture capital, primarily for human medical interests. By January 1, 1992, Amgen, one company of these origins, joined the Standard & Poor's 500 and was given a $10 billion market evaluation.

The growing market of biotechnology-based protein drugs is now well-over $2 billion annually. In the late 1970s, interest in animal applications of biotechnology started to attract investments. Bovine somatotropin (BST) product development was the first direct spinoff of this early drug research activity. Many other applications of biotechnology for animals and plants have subsequently been the basis of the formation of small companies. Federal agencies directed close to $4 billion to support biotechnology research in 1992; this is of special interest to those of us interested in animal production and the development of improved methods for enhancing the efficiency of production. Even more than that is being spent by hundreds of companies to develop further scientific bases and applications of biotechnology. Of tremenendous potential for broadening the horizons for many aspects of biological research is the 15-year, $3 billion federal support of the Human Genome Project.

BIOTECHNOLOGY ADVANCES IN HUMAN MEDICINE AND SPINOFFS TO ANIMAL AGRICULTURE

Others in this conference will undoubtedly discuss the numerous and essential contributions of animal models to the development of human drugs and

treatment strategies for even the most intractable of the human disease conditions. The following discussion will deal with certain aspects of the applications of biotechnology to animal research and agriculture.

In Table 1 is a list of protein drugs approved by the Food and Drug Administration (FDA)since 1982, starting with Humulin®, a biosynthetic insulin *(Genetic Engineering News,* January, 1992). Momentum in protein drugs is growing—5 of the 30 products approved by the FDA in 1991 were of this type. This rate may be duplicated in 1992 and possibly 100 more biotechnol-

TABLE i: BIOTECHNOLOGY-BASED DRUGS APPROVED BY FDA

Product	Company	Indication	Year
Actimmune	*Genentech*	*management of chronic granulomatous disease*	*1990*
Activase	*Genentech*	*acute myocardial infarction*	*1987*
		acute pulmonary embolism	*1990*
Alferon	*Interferon Sciences*	*genital warts*	*1989*
Engenix	*SmithKlineBeecham*	*hepatitis B*	*1989*
Epogen	*Amgen 2*	*treatment of anemia associated with chronic renal failure, including patients on dialysis & not on dialysis, and anemia in Retrovir-trated HIV-infected patients*	*1989*
Procrit	*Ortho Biotech*	*treatment of anemia associated with chronic renal failure, including patients on dialysis & not on dialysis, and anemia in Retrovir-trated HIV-infected pa lients*	*1990*
Humatrope	*Eli Lilly*	*human growth hormone deficiency in children*	*1987*
Humulin	*Eli Lilly*	*diabetes*	*1982*
Intron	*Schering-Plough*	*hairy cell leukemia*	*1986*
		genital warts	*1988*
		AIDS-related Kaposi's sarcoma	*1988*
		non-A, non-B hepatitis	*1991*
Leukine	*Immunex*	*autologous bone marrow tranplantation*	*1991*
Prokine	*Hoechst-Rooussel*	*autologous bone marrow transplan-tation*	*1991*
Neupogen	*Amgen*	*chemotherapy-induced neutropenia*	*1991*
Orthoclone OKT3	*Ortho Biotech*	*reversal of acute kidney transplant rejection*	*1986*
Protropin	*Genentech*	*human growth hormone deficiency in children*	*1985*
Recombovax HB	*Merck*	*hepatitis B prevention*	*1986*
Roferon-A	*Hoffman-LaRoche*	*hairy cell leukemia*	*1986*
		AIDS-related Kaposi's sarcoma	*1988*

ogy-based drugs are now in clinical trials. Applications of identical or similar products for animals are bound to follow all of this activity. A major advantage of this is that human drug development leads to initial reagents and test probes for studies both *in vitro* and *in vivo* in other animals.

Of longer-term consequence is the development of a large number of products resulting in significant production process developments and associated discoveries which lead to reduced costs of drug production. In many cases, this alone permits consideration of new animal product concepts. Additionally, some of these biosynthetic proteins are likely to have desirable effects during certain physiological states of animals not predicted from their names or the initial basis for their discovery.

The rapid development of genetic engineering has made it possible for a soaring rate of new discoveries. Proteins present in minute quantities, but occasionally of immense importance to animal physiology, can be predicted from messenger RNA. Thus, the existence of previously unknown proteins can be demonstrated by isolation and multiplication of very specific genetic codes. This has led to the discovery of numerous important proteins (i.e., hormones, receptors, enzymes) that otherwise would have been impossible to discover by classical endocrinology-based techniques, even before knowing the function of these proteins.

Within the lifetimes of many of us, the understanding of receptors on cells have evolved from essentially a concept to a specific protein or a family of proteins. These advances have, in many cases, replaced the need for pharmacological classifications for receptor types such as the adrenergic receptors which are subdivided according to their pharmacological response to epinephrine and non-epinephrine (Ahlquist, 1948). The genetic expression of a hormone receptor and binding characteristics of each of a family of receptor proteins can now be studied for cell type specificity, etc. (Laird et al., 1991). The diversity of protein receptors has led to new strategies for drug design including the utilization of very powerful chemical tertiary structure software for predicting specific drug analogs with highly selective activity. In some cases, possession of quantities of a specific receptor protein allows screening for specific binding by peptides or other chemicals to develop specific blockers.

As recently reported (Gibbons, 1992), second generation products from biotechnology will include other specific means of modifying selected protein expression. The expression of specific proteins which either inhibit growth enhancement or cause disease conditions may be reduced or eliminated by blocking the transcription of DNA into the specific protein messenger RNA. Another method of obtaining similar responses is to develop short oligonucleotides that recognize and bind to specific messenger RNAs and thus block protein synthesis. These and other means provide opportunities for developing drugs that enhance animal production and health.

SUMMARY

Human health-related research is leading the way to new technological breakthroughs, reagents, probes and general understanding of biological systems at a molecular level. An additional benefit will be the generation of many opportunities for enhancing animal production. In many cases, species specificities may be engineered into the developing strategies to ensure that human health concerns are met even at a molecular level. At the present time there are more opportunities for improving the efficiency and endproduct quality (e.g., nutritional value), than can be funded by most major companies. The many exciting advances in biotechnology are steadily making the discovery process more affordable and allowing the backlog of opportunities to build. Recognition and acceptance of how to safely apply biotechnolgically based productivity enhancers and health aids will surely result in much greater investment in animal drug development in the near future. All of this activity, plus the advances in animal science, will assure the world new methods of increasing the abundance, quality and variety of foods. Given the prediction that 10 billion people may be on earth within the first half of the 21st century, this is an issue of great importance. These future products will be cheaper and safer to produce and will lead to superior, safer and environmentally friendly management options for animal agriculture. All of these qualities should make these innovations available to more of the world's food producers including those in developing countries.

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