On Research and Patenting

When science and legislation meet

by Ben Fohner

Just over 30 years ago, during a lull in a bacterial plasmid conference, Dr. Stanley Cohen and Dr. Herbert Boyer, researchers at Stanford and UCSF respectively, were chatting over sandwiches in a Waikiki Beach restaurant. As the conversation turned toward their areas of study (plasmid DNA for Cohen and restriction enzymes for Boyer), the scientists began to realize the complementary nature of their research. They wondered if by combining their methods for cleaving DNA and manipulating plasmids, they could insert foreign DNA into circular plasmid DNA and then insert that plasmid into a living organism. Returning to the Bay Area, they began to integrate their work and after only a year. In November of 1973, they published their discovery of a method to manipulate and re-insert DNA into microorganisms, the first such procedure.

Dr. Stanley Cohen co-discovered recombinant DNA technology.

Patenting the Cohen-Boyer Discovery

Although they initially did not apply for a patent because of their reluctance to commercialize the process, after speaking with Niels Reimers, a technology transfer professional at Stanford, they decided to apply for a patent one week before the filing deadline. Eight years after filing for the patent with the United States Patent and Trademark Office and after numerous ethical debates that included a National Academy of Sciences international convention held specifically to discuss the technology, the patent was granted in 1980.

Since the granting of the patent, the Cohen-Boyer discovery has been an incredibly successful and integral technology. Called recombinant DNA technology, this biochemical process is a major underlying foundation of the biotechnology industry. The primary reason for its widespread success lies in its extensive applicability, with uses ranging from agricultural modification of pest-resistant plants to pharmaceutical synthesis of human cellular products.

Stanford's Office of Technology Licensing

Carrying the DNA technology through the tedious patent process and helping to balance ethical issues with profits was the responsibility of the Stanford Office of Technology Licensing, the office that organizes all University technology transfers. This office was established in 1969 after the signing of the Bayh-Dole Law, which gave universities the first right to any discovery developed using its resources. The Stanford Office of Technology Licensing promotes "the transfer of Stanford technology for society's use and benefit while generating unrestricted income to support research and education." Since its creation, the OTL has disclosed nearly five thousand new technologies, generating nearly 550 million dollars with about 475 million of that going directly back to the University and the inventors. Typically, the University reinvests this money back into the research occurring on campus. The Cohen-Boyer discovery alone accounts for nearly one-third of the total amount earned by Stanford patents. By transferring new technologies from the University inventors to the public, the OTL insures that society benefits from innovations at Stanford and that the University benefits monetarily from the research that takes place on campus.

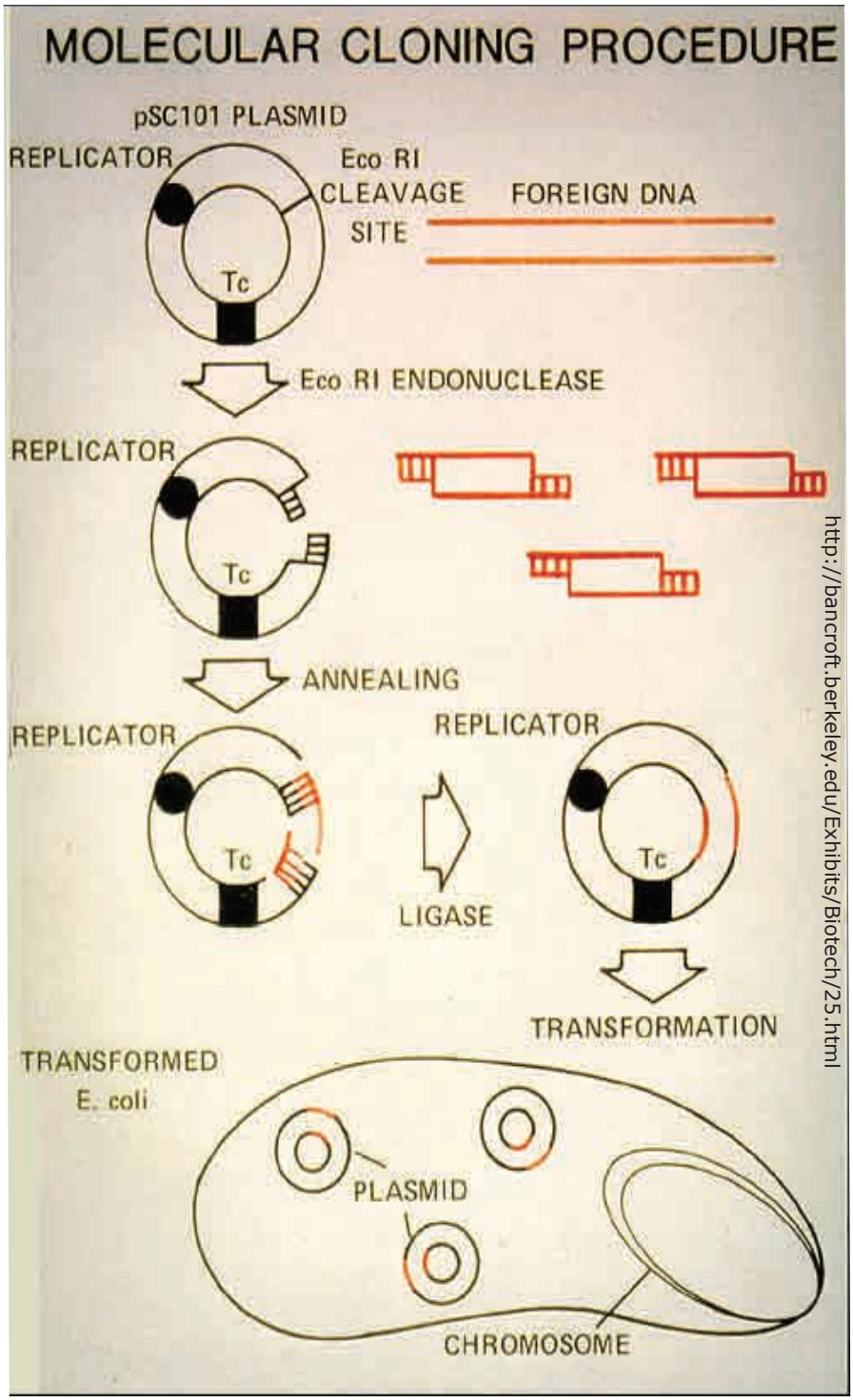
Typically, the office receives about one invention disclosure every day from people working at Stanford, usually patenting about fifty percent of these submissions. According to Kathy Ku, the director of the Office of Technology Licensing, biotechnology accounts for "about half of these disclosures and usually ends up

being significantly more profitable in part because it is much less likely to be phased-out." After reviewing the application and meeting with the inventor, the licensing professional assesses whether or not the invention has the potential to create meaningful income for the University. If so, the office begins the patenting process and, after receiving a patent, begins marketing the invention to the public.

Making the Technology Public

The final step in the transfer of the technology from lab bench to commercial interests is one of the most controversial steps in the development of biotechnology. The extreme costs and risks associated with the research and development of a biotech product, usually amounting to "between 200 and 350 million dollars (U.S.)" and "7 to 10 years of development" (Harvard v. Canada SCC 20), makes the patent and licensing system "the only protection available for the intellectual product of this research, and thus, the only hope of a fair return against the great financial risks that investment in biotechnology entails" (Harvard v. Canada SCC 24). Because of the extremely high research costs and risk of failure, developers must aggressively license the technology just to meet costs and satisfy shareholders. According to Kathy Ku, commercial entities are much more concerned with profit and end up seeking broad patents on everything that they discover, a necessary strategy in a field requiring such extensive initial investment.

Ethicists like Dr. David Magnus, co-director of the Stanford Center for Biomedical Ethics, feel that this profit-maximizing patenting and licensing of biotechnology, more specifically of genes, often stifles research and prevents public benefit from the technology. One example of this can be seen in Miami Children's Hospital's policy regarding Canavan's disease research. In this case, the Ashkenazi Jewish people, who donated their tissue to further research into this neurodegenerative illness, were prevented from benefiting from the therapy that the hospital developed by the extra costs imposed by the licensing system. Another example, can be seen in the Bogart Triple Test, a blood test used to determine the probably of Down syndrome in the fetus of a pregnant woman. In this case, the discoverer of one aspect of the test, had used his patent privileges to set up



Molecular cloning involves inserting foreign DNA into a circular DNA plasmid

a company to perform all of his tests, and if the patent holder for another aspect of the test had done the same, nobody would be able to perform the full test without some sort of compromise. In other words, if multiple patents addressing the same issue overlap, medical tests and procedures can be made ultimately impossible. A third theoretical example can be seen in a company that held an exclusive patent to perform a type of procedure that was a necessary component of further research. Without the permission of the company, any research involving this foundational procedure would be illegal, an outcome that could have a drastic impact on research reliant on existing technology.

Making the Technology Affordable

In the case of the Cohen-Boyer discovery, the Stanford OTL was able to use a liberal, research-oriented approach to license the technology, a strategy that paid off both monetarily and ethically in that the profits derived by Stanford but did not inhibit widespread use and benefit from the technology. According to Niels Reimers, the former director of the Stanford OTL, the "objectives [of the OTL] were to develop a licensing program consistent with the public service ideals of the university, to encourage the application of genetic engineering technology for public use and benefit, to minimize the potential for biohazardous development, and finally, to provide a source of income for educational and research purposes." Thus, Stanford elected to license the recombinant DNA technology to an unlimited number of companies, making it "cheaper to take a license than to fight" for companies "big and small, rich and not-so-rich." Through a combination of flat fees and a very modest 0.5% royalty, the OTL was able to devise a licensing strategy where "pretty much any company could afford" the technology. Because the Cohen-Boyer discovery "was really broad technology," the OTL determined that giving the technology to one company would probably be neither smart business nor smart use of the technology."

Gene Patenting and Commercial Interests

The Cohen-Boyer patent was an extraordinary discovery that allowed for ethical considerations to be taken into account and showed that such considerations can coexist with the need to finance research and make a profit. To ensure that these compromises are made, the practice of patenting and licensing biotechnology should change substantially. One particularly problematic issue is disease gene patenting. According to Dr. Magnus, disease gene patents are a form of biotech patenting akin to observing an object, such as a gene, and then patenting the process of "look[ing] at this object in any way using any process." This "crazy" notion would be akin to using a microscope to look at a particular cell and then patenting any method of looking at that cell. The American Medical Association code of ethics "prohibits patenting of procedures" because such patents could inhibit doctors from practicing medicine.

The fundamental difference that Dr. Magnus sees between disease gene patenting and the patenting of other forms of biotechnology is that other forms require extensive research to bridge a fundamental gap between the original and end products. He argues that patents such as these other forms are necessary to promote research and that, although imperfect, no other system exists that can match the amount of money that the current patent system allows to be reinvested into research and development. Dr. Magnus feels that legislative action, while helpful, is highly improbable as a means of solving the ethical concerns of disease gene patenting. Rather, he feels that by applying a significant amount of pressure on companies through "public awareness, awareness within the medical community of the problem, and awareness by the disease suffers who are stakeholders in the research," corporations may voluntarily adopt the AMA code of ethics, thereby alleviating the problem. Additionally, the awareness of disease sufferers could give them "a better bargaining position" in the biotech industry, promising better access to technology. This fundamental change in the biotech industry will be difficult to accomplish, especially with the profit-driven nature of commercial enterprises. Even at research universities, where the goal is to promote public knowledge and well-being, more and more researchers are "try[ing] to raise revenue" and become "more aggressive" with patents than private companies. Despite the current complications and difficulties in balancing public access with profit, the Cohen-Boyer licensing strategy provides a positive, guiding example of the balance between ethics and profit motives. S