BIOTECHNOLOGY

DNA dollars

Linnaea Ostroff examines a history of Genentech, the US company that first made biology a business.

As the mysteries and mechanics of DNA were being revealed, it was unclear whether the molecule would be used for good or evil. Debates raged: utopian fantasies of ending disease and famine competed with fears of mutated life forms running amok. A suitably startling, if less popcorn-worthy, event occurred in October 1980, when the promise of DNA modification raised US$35 million in a landmark initial public offering (IPO), which saw the fastest stock-price rise in the market's history.

The record-breaking IPO was that of Genentech, a small company based in San Francisco, California, whose plan was to produce drugs using recombinant DNA technology. This was the first commercial manipulation of DNA and the first sale of biological science as a commodity in its own right. The biotech industry was born. Genentech's unique corporate structure, which blurred the boundary between academia and industry, was swiftly imitated. The sometimes uncomfortable entanglement of publicly funded basic research with private business enterprise persists to this day.

Genentech by science historian Sally Smith Hughes gives a detailed account of the founding and early years of the company. Much of the material in the book comes from oral histories collected by Hughes, along with written archival material. Hughes's book is not, however, a journalistic analysis of a unique and important company: it is an account of the key players, as told to a sincere admirer.

"Although Genentech's business model was groundbreaking, the long-term strategy was a classic risk."

Nevertheless, Genentech's achievements in science, medicine and business were momentous. One of the company's co-founders, Herbert Boyer, a molecular biologist at the University of California, San Francisco, was at the time a leader in the development of recombinant DNA technology. Boyer and others had recently discovered a means of reorganizing (recombining) the sequence of DNA molecules, and were pursuing a method to use this engineered DNA to generate proteins. This had profound implications for drug production and development.

Whereas most drugs had been discovered by large-scale screening of synthetic chemicals, a handful, such as insulin, were natural proteins whose production in the body was impaired in diseases such as diabetes. Proteins have exceptionally complex structures, and it is still too difficult to routinely synthesize them from scratch. Therapeutic proteins were at the time sourced from animals' organs and human cadavers, making their supply and safety unreliable. In theory, recombinant DNA could provide a safe, consistent source of this class of therapeutics.

Genentech: The Beginnings of Biotech
SALLY SMITH HUGHES
University of Chicago Press: 2011. 232 pp. $25, £16

Boyer's group was working on a way to coax bacterial cells to produce therapeutic proteins from recombinant DNA. More importantly, recombinant DNA presented a means of designing drugs using the biological mechanisms of a particular disease, which seemed to be an obvious advance over the pharmaceutical industry's random screening procedures. Hughes does not, however, touch on any of this, leaving the reader to wonder why recombinant DNA is viewed as so useful.

The reasons the IPO was so successful, and why that success was so shocking, are also underdeveloped in the book. At the time it went public, Genentech had the intention of making pharmaceuticals but had no actual drugs in the pipeline. What it did have was a contract with Eli Lilly, the largest producer of synthetic insulin. The contract was the first of its kind: Eli Lilly was not paying Genentech to produce insulin, nor licensing a method to do so, but was paying it to do the basic scientific research needed to develop a method. Never before had an independent group of scientists contracted with a for-profit organization to make basic scientific discoveries, nor had a publicly traded company offered research as its sole source of revenue.

➲ NATURE.COM
For a review of the US biotech debate:
go.nature.com/yv1ffo

A patent on recombinant DNA techniques was granted in 1980 to Stanford University, California, and to the University of California, where Boyer and his colleagues had developed the technology. The assurance of intellectual-property protection for genetic-engineering methods and products encouraged the explosion of the biotechnology sector, as academic researchers began to independently commercialize their findings. The now commonplace practice of scientists maintaining ties to both universities and their own associated companies, along with the conflicts it creates, comes directly from Genentech's initial arrangement.

Although Genentech's business model was groundbreaking in its mechanics, the long-term strategy was a classic risk. Genentech's insulin was intended to be the Gutenberg Bible of recombinant DNA technology — an established product made in a new way with a guaranteed market. Yet the route between basic knowledge of a disease process and an effective therapy is punishing, and many subsequent designer drugs generated using the method proved not to be viable.

Rational drug design has not overtaken traditional drug-discovery approaches, and biotechnology development is shifting back to large pharmaceutical companies, which can hedge risk internally — although the future of drug discovery is a legitimate concern. Genentech itself is now wholly owned by Swiss pharmaceutical giant Roche.

The scant objectivity, the somewhat plodding chronology of unfolding events and the sparse explanations of technical terminology in Hughes's account aside, Genentech's story remains a compelling one. It neatly reveals the divergent challenges of basic science, medical science and business, and despite its novelty, the tale illustrates several enduring principles of science and markets.

In shifting genetic-engineering research from academia to industry, Genentech and the industry it founded accelerated the development and distribution of medically and agriculturally valuable products. It triggered practical decisions on policy and regulation, while effectively sidestepping philosophical and ethical questions about the uses of DNA: the market would decide what DNA should be used for. Genentech's business model shunted private money directly into basic research, drew investors into basic science and academic scientists into business. Even as the industry reorganizes, these relationships remain. ■

Linnaea Ostroff *is a researcher at the Center for Neural Science, New York University, New York 10003, USA.*
e-mail: lostroff@nyu.edu