

Biotech's roots



Genentech: The Beginnings of Biotech

Sally Smith Hughes

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Reviewed by Phillip A Sharp

Common lore states that there is no history, only biography. Sally Smith Hughes's new book on Genentech is an important addition to the history of biotech. *The Beginnings of Biotech* follows the creation of Genentech by the venture capitalist Robert Swanson and the scientist Herbert Boyer. Although the book tells the story of the birth of biotech from the perspective of Genentech, it is a good read because it focuses on the people and science on the West Coast from which the industry grew.

The story opens with the science of Stanley Cohen and Boyer in the 1970s that led to the highly remunerative patent covering the uses of recombinant DNA. Cohen, an expert in drug-resistant plasmids, and Boyer, an expert in restriction endonucleases, met at a conference in Honolulu in 1972 and decided to collaborate on making recombinant molecules. Their first paper was published in 1973 and led to the subsequent experiment involving John Morrow, a graduate student from Paul Berg's laboratory, that formed the basis for the patent. That Cohen and Boyer got the patent and Paul Berg got the Nobel Prize in Chemistry is an unresolved issue in the book. Hughes focuses on the story behind the patent; it remains for someone else to tell the other story.

Swanson is the hero of Hughes's story. He clearly saw the potential of biotechnology to generate important new products and profits. At the time of the establishment of Genentech, he was recently unemployed but fascinated by recombinant DNA, at least partially through contact with the former company Cetus. A cold call to Boyer and a couple of beers created the first biotech company. Hughes, with passion and sensitivity, tells how Swanson, supported by venture capitalist Tom Perkins, led the struggling new start-up. The first objective was the exclusive right to the Boyer-Cohen patent, which would have blocked the formation of competing companies. This was not successful. The second was demonstrating the power of Genentech's technology. The company started in academic labs at the University of California, San Francisco (UCSF), City of Hope and Caltech. This made for complications later but illustrates the power of collaboration in getting some-

thing done as soon as possible. At this stage, many names linked to the early days of Genentech enter the story, including Robert Crea, Herb Heyneker, Peter Seeburg, John Shine, Axel Ullrich and David Goeddel.

Boyer and Swanson first decided to clone synthetic oligonucleotide sequences for the 14 amino acids of somatostatin and purify the protein from bacterial extracts. The synthetic DNA oligomers were made by Keiichi Itakura of City of Hope and some by Richard Scheller at Caltech. Arthur Riggs, also at City of Hope, worked with the Boyer-led Genentech team to assay the hormone. At the same time, the teams took on the synthesis of human insulin A and B chains. The tension in the story builds as the initial capital decreases and the hormones are not delivered. In the end, Genentech is launched, but some years later City of Hope and Genentech were locked in litigation over the extent of royalties due to the former for the early technology patents from these projects.

Although not mentioned by Hughes because of its minor role and probably the suppressed memories of Swanson, I witnessed a piece of the early moments of Genentech. In 1977, a venture capital firm, INCO, invited me to consult on an external investment in Genentech. At the meeting, Swanson, Boyer, Itakura and Riggs made the pitch in the offices of Kleiner Perkins of producing somatostatin and insulin as the immediate objectives of the company. INCO made the investment, but later Swanson demanded that INCO divest of its Genentech equity when it led the establishment of a competing biotech company, Biogen.

The race to clone the gene encoding insulin is a major part of the story. As it unfolds, Genentech is in negotiations with Eli Lilly and other companies, and Walter Gilbert of Harvard, funded by Biogen, is leading a competing team, and another team at UCSF led by Howard Goodman and Bill Rutter is also in the hunt. Lilly bets on two horses and signs an agreement with both Genentech and UCSF. Another fascinating story is the migrating cDNA clone for human growth hormone. As Hughes tells it, Axel Ullrich and Peter Seeburg took the clone to Genentech after a midnight raid on John Baxter's freezer at UCSF. The question of the importance of this clone in the success of Genentech's cloning of the gene encoding human growth hormone was a matter of litigation that ultimately produced a new building named for Genentech at UCSF.

Hughes's book ends with the amazing initial public offering of Genentech, when the stock opened at \$35 and soared to the mid-\$80s in a minute. This reception set the table for the future funding of biotech by Wall Street. Hughes's book is an important contribution to the history of the field, and I expect that there will be many other contributions. Critics may argue that Hughes does not adequately cover the early origins or the social implications of biotechnology. However, I enjoyed this part of the history of the industry and recommend it to both scientists and laymen.

COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.

Phillip A. Sharp is at the Koch Institute and Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA.
e-mail: sharppa@mit.edu