From Lab Bench to Wall Street

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Editor’s Note:

In addition to publishing traditional Book Reviews, the FASEB Journal will publish, under our “Milestones” rubric, book-notes and/or memoirs written by the authors themselves. We invite our readers who are authors of books for the general reader to write about their work in the form of informal essays, memoirs, etc. Our first booknote/memoir is by Tamas Bartfai, Ph.D., who is the director of the Harold L. Dorris Neurological Research Center at The Scripps Research Institute, La Jolla, California. Professor Bartfai is former head of central nervous system research at Hoffman-La Roche, Basel, Switzerland, and spent most of his professional career at Stockholm University. His essay explains the genesis of his new book, Drug Discovery: From Bedside to Wall Street, co-authored with Graham V. Lees (2005, Academic Press/Elsevier).

Why write a book on drug discovery, a book that is neither fiction nor textbook? Well, the past three decades have changed the way biomedical scientists view themselves. Our desire to understand the key processes of life—and of winning scientific prizes—has now been complemented by an increasing desire to help discover drugs that are clinically and economically successful. These decades have coincided with an enormous expansion of basic biological science in academia where we’ve seen, for example, the advent of genetic engineering, the deciphering the human genome, and the discovery of cell-death as a defined mechanism. In society as a whole and within the pharmaceutical industry we have witnessed an unprecedented increase in spending on drugs, in drug discovery, and in the testing and marketing of new medicines—a trend that may or may not be likely to continue.

As a result, the pharma industry emerged as a very strong economical factor with capital and earnings comparable to or better than that of traditional large industries such as shipbuilding, automobile manufacturing, or electricity generation. There is of course one big difference, the price per earning ratio of traditional industries is 4:1, whereas that of pharma is 13:1! This reflects the uncertainties of the product development process in the pharmaceutical industry as well as the windfall profits resulting from the rare successes such as the statins. These drugs have been found to be so safe and effective that they can be sold to tens of millions of people to be taken daily for the rest of their lives. It’s a safer, more sustainable business with sales every day and more reliable than selling newspapers. So many academic researchers want to be part of an enterprise where one discovers new drugs, treats diseases (but, sadly, cures mighty few) and, perhaps incidentally, becomes very rich. The spectacular success of a few biotech companies—mostly those who have developed biological agents such as GH, tPA, β interferon, or vaccines—has fueled the dream.

Now universities and government agencies (vide the NIH Blueprint) are also itching to develop drugs. The problem is that only a few of their cadre have a sufficient overview of the drug discovery process. It is not only tortuous but highly risky in terms of human suffering and in its potential for a huge loss of money.

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That is not to say that a large number of academic researchers do not already act as consultants to the pharma industry, indeed they are used often and successfully. However, they are called in to answer a specific question, to solve a specific technical problem, and to give an opinion based on their deep, if narrow, knowledge. They are not given an overview of all the projects in all the areas of disease that are simultaneously being studied in the same company two doors down on the corridor. These projects, even if not scientifically parallel or even in the same disease or diagnostic area, may be internally competitive and their success may be the death of the academic consultant’s program even if that program is a scientific and technical success.

On the other hand, one can’t open a major newspaper without finding daily reports from the pharma-basher front: new drugs introduced and withdrawn, whistle-blowing in industry or regulatory agencies, promos for zealous interest groups, and anxious lawmakers. Then there are the ethicists who wonder how many drugs should be developed that prolong life by three months at a price that might pay for the vaccination of 2000 children. One the one hand, when the government, rich philanthropists like Gates and Ellison, and advocacy for the poor like the Amman fund, all urge us on to develop new drugs, everyone picks up a broad, if superficial, appreciation of modern therapeutics. On the other hand, this received wisdom is shaken when, say, the government muscles aside merger candidates, or when there is a flu-vaccine shortage, or when trial lawyers file class action suits against big pharmaceutical companies. Of course, this turmoil leads to the rapid populist success of books that explain or simply denounce that old devil, Big Pharma. The critics claim Big Pharma endangers us, overcharges us, and, worse yet, supports an even worse devil, the lobbyist.

In this pharma-bashing climate, why would a basic neuroscientist write a book about drug discovery? I am not a physician; I cannot heal. But I have had the great fortune to be involved in the development of medicines that are useful and used broadly—first as a university researcher acting as a consultant in projects where the hope of success was low, where the internal competition was unknown to me, and where the personalities of all the actors in the drug-development play seemingly overshadowed the plot. Yet, drugs came into being and the small, unknown Swedish company Astra was able to beat out international giants such as Glaxo and Smith-Kline Beecham by simply making a novel and better drug to control heartburn—Losec. Heartburn does not exactly sound like the epitome of medical need, but if I add that the use of surgical theaters fell by 75% as gastric surgery became less and less necessary, and since no surgery is risk free, then you might see that heartburn is no small potato. A proton-pump inhibitor that directly addressed the acid was better than the histamine H2 blockers of the two giants. That, and the fact that the new, and now dominant class of antidepressant drugs, the SSRIs, was born at the same time at this small company—Zimelidine was the forerunner of Prozac, Paxil, etc.—sold me on drug discovery. All (i.e., 99% of my colleagues) who reached tenured full professorship in Sweden stayed on as professors and consultants, but I was willing to take the big step of leaving a chairmanship for an apprenticeship in pharma. I spent years at one of pharma’s best schools: Roche, a Swiss, research-driven company with great medicinal chemists and excellent biologists in New Jersey, Basel, and Palo Alto. Roche made the first blockbuster ($1 billion/yr)—Valium. It had enough foresight to buy the patent on PCR and to acquire the controlling interest of the large biotech Genentech—whose birth I had witnessed from Sweden through Bertil Aberg’s discussions—as he made the first investment in Genentech from Kabi/Kabigen in Stockholm.

It was an exciting time and an exhausting one. I continued my research work on the basic problem of fever, which is of no interest whatsoever to drug companies—no matter, how I can explain its beauty? “Aspirin, Tylenol” is all they repeat. So when I left pharma without being fired, or going to a biotech company, and came to The Scripps Research Institute (TSRI) and also to the Karolinska Institute, I was a rare bird. (As a former pharma executive, one is no longer of interest to colleagues in academia by virtue of one being no longer able to dole out research funds, support dinners, and meetings, etc.)

Happily, TSRI is highly entrepreneurial. Many colleagues have started biotech companies and even more are consultants to large industrial concerns and act as advisors to regulatory agencies, to NIH, and to venture capitalists. In doing so they are assumed to have seen the whole process of deciding which disease to treat, which target to aim at, with which molecule, at what risk:benefit ratio, in which competitive climate, and at what price. And, of course, they know many of these answers, and they do extremely well—judged from how often people bearing capital come back to them for more advice.

Judge my surprise, then, when in the corridor of TSRI, a Nobel Prize-winning chemist caught me by the elbow and inquired “How can they (the pharma sustaining his lab) no longer want the antiviral they supported me for years to make? It does not make sense.” “Explain it to me!” he demanded. “Well,” I said, “perhaps the competitors got ahead of you, perhaps the virus has mutated, perhaps they will get out of antivirals all together, perhaps your contact has been promoted and cannot deal with this project, or perhaps he or she has just been fired.” “These are not chemical arguments” he hissed, and he is right, they are not.

As a direct result of this illuminating encounter, I gave three crowded lectures to an eager audience of chemists and biologists, graduate students, and professors, venture capitalists, and biotech executives. Indeed, even some of my big pharma colleagues showed up. They did not want to know my views on fever—it was the ins and outs of drug discovery that interested them. The audience that was there was one that would...
willy-nilly come to interact with, or work for, the pharma industry, an enterprise that, despite its many problems, remains a formidable research machine with many great achievements. Dr. Graham Lees, a neuroscientist by training and an accomplished science publisher, took the material of the lectures, replete with my personal biases and values, added some of his own, and more besides, and together we produced a boiled-down version of those lectures at Scripps and called it *Drug Discovery: From Bedside to Wall Street*.

We hope that this book—or more likely parts of it—will be read by many people from many walks of life, because health care—of which drugs are a very effective and ever expanding part—is the business of all of us. Readers of multidisciplinary publications such as The FASEB Journal are among the main targets of this book because their interest and their training permit a critical and, hopefully, constructive reading of our exposition, written as it is from a scientific rather than a pharma-bashing or promotional perspective. Our society will not be better off if the pharmaceutical industry is discredited beyond repair by the pharma bashers or if the regulatory agencies succumb to the pressures of unreason. Drug discovery is an enormous research enterprise with strong economical incentives. Closer to us than the space program in its claim on our psyches, drug discovery deserves our support, even if it is not as spectacular as that trip to Mars.