BOOKS: BIOTECHNOLOGY

A Genetic Code Napoléon?

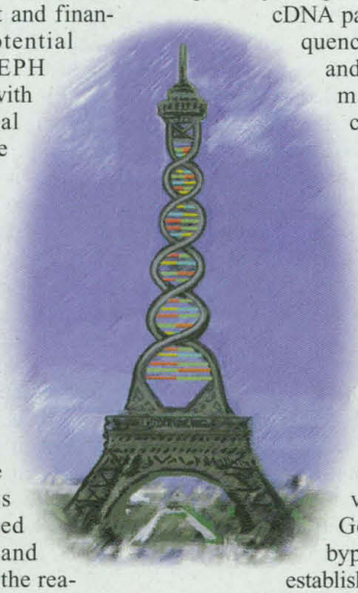
Wilhelm Ansorge

We have heard about the French connection, the French Riviera, French wine and cheese, and the French kiss. But the title of *French DNA*, Paul Rabinow's new book, poses a puzzling question: Can a country claim to have its own genetic material? In this account of the collapse of an agreement between a French institute and an American company to collaborate on efforts to discover diabetes genes, Rabinow demonstrates that the answer to this question is far from simple. The answer is entangled in a complex historical context, one formed from the interactions of ethics, national pride, personal versus institutional interests, the search for scientific glory, and visions of financial rewards. The story Rabinow tells is further complicated by the pitfalls of managing a scientific institute during stormy times and under the strain of a global race toward an ambitious goal: the first map of the human genome. The outcome was also significantly affected by the personalities and characters of the scientists involved. This mixture of ingredients provides the material and setting for a good drama.

French DNA
Trouble in Purgatory
by Paul Rabinow
University of Chicago, Chicago, 1999. 209 pp. $25, £17.50. ISBN 0-226-70150-6.

Several exceptional achievements form the background to the events discussed in the book. One was the construction and operation of the Généthon, an innovative "factory to find genes" that was up and running in a Paris suburb by the end of 1990. This joint enterprise of France's premier genomics laboratory, Centre d'Etude du Polymorphisme Humain (CEPH), and the powerful and well-established dystrophy patients group Association Française contre les Myopathies (AFM) marshaled the complementary visions, skills, and financial powers of a group of particularly dynamic people. As a result, the CEPH (led by its scientific director Daniel Cohen) succeeded in producing the first physical map of the human genome by the end of 1993. The map, together with the important bank of reference human DNA organized and maintained at the CEPH, gave the French institutions a highly visible position and a significant advantage in the genomic field of the time.

Thus it came as no great surprise when, in 1993, the U.S.-based biotechnology company Millennium Pharmaceuticals and the CEPH developed plans for a collaborative effort to study the genetic basis of non–insulin-dependent diabetes. The objectives of this collaboration could have been medically significant and financially lucrative. The potential partners agreed that CEPH would supply Millenium with a bank of genetic material collected from a large number of French families, and Millennium would provide funding and expertise in new technologies to accelerate the identification of the genes. The French government initially approved the terms of the agreement. But in early 1994, just before the agreement was to be signed, the government reversed its prior approval and decided to stop the negotiations and the collaboration. Among the reasons it cited was the reluctance to give away the genetic material collected from French families—the French DNA—to an American company having commercial purposes. Rabinow describes and discusses the circumstances leading first to the potential agreement and then to its collapse (another type of "Millennium crisis"), and he illuminates the complex relations between genetics, bio-ethics, patient-interest groups, venture capital, and the French government. The author, a professor of anthropology at the University of California, Berkeley, saw himself as a philosophical observer whose main task was "to identify the crystallization of value judgments around new forms" in the emerging fields of genomics and biotechnology.



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Among the issues Rabinow takes up is the transfer of technology from scientific institutions to start-up companies and industry. It seems that one explanation for the failure to finalize the Millennium deal was the late awakening of France (and many other European countries) to the potential importance of genomics and biotechnology for national prosperity. At the moment of the decision, a thorough understanding and analysis were not available and the government suspected it might be giving away much more than it was getting in return; refusal was considered the safest solution. These days, international negotiations and global deals are better prepared and more common.

Rabinow's account reveals that the institutes and scientists involved recognized very early on the importance of such issues as techniques for the large-scale, simultaneous analysis of gene expression in various tissues, analysis of multiple signaling pathways, sequencing of parasite genomes, cDNA patents, storage of DNA sequences in the public domain, and ownership of biological material. The author discusses such issues as hierarchical research structures, north-south global scientific collaboration, and women's rights in the laboratory—issues that were not considered important in Europe at that time.

The book also provides interesting observations about organization and life at scientific institutes. The unconventional set-up of the Généthon and its financing bypassed the relatively rigid, established process in French science; therefore Généthon was not immediately understood or cheered by everybody in the field. Although the importance of personalities in scientific conflicts is generally well known, it is still surprising to observe the extent to which they influenced the outcome of this story. Rabinow's remarks on management of the workplace are an every day reminder to all of us: Providing little information to employees, for example, usually breeds a high level of gossip, and a methodical approach is usually preferable to playing firefighter through a crisis.

After reading the book in search of the answer to the question I posed at the beginning, it seems "French DNA" initially described and meant the human DNA collected in France. In the heat of the numerous written arguments over the proposed CEPH-Millennium collaboration (many of which appeared in the popular press), the longer and more exact phrase was simply abbreviated. Nonetheless, one can expect to find in every country some people who would take a nationalistic view of DNA.

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The wide variety of subjects that Rabinow treats guarantees the interest of a large group of readers: students, researchers, scientific managers from academic institutions as well as from industry, politicians, and interested laymen. *French DNA* certainly will be of interest to venture capitalists. And because of the author's frequent inclusion of French phrases, his book is also a pleasant way of refreshing one's school knowledge. *Bonne lecture!*

TELEVISION: MICROBIOLOGY

Mega Roles for Microorganisms

Caroline S. Harwood and E. Peter Greenberg

Those of us who have tried to explain to a family member that microbes are in every breath we take and on every surface we touch, that all life depends on them, and that, no, most won't kill you, know that microbiology can be a tough sell. *Intimate Strangers: Unseen Life on Earth*, a four-part series premiering on the Public Broadcasting Service this month, informs us "we are not the true masters of life on Earth. Microbes are." Beautifully photographed at locations ranging from the coast of Oregon to a farmer's field in Zimbabwe, the series conveys general concepts more than specific information. The programs, produced with the assistance of the American Society for Microbiology, are meant to be interesting and informative to both scientists and non-scientists. The series tells the tale of the microbes through a set of small stories, which are often told by scientists. These vignettes capture the sense of scientific adventure and the personalities of the scientists themselves. To help explain concepts that might otherwise make the eyes of a general audience glaze over, the programs use clever animation and well-drawn metaphors from everyday experience.

Intimate Strangers
Unseen Life on Earth

Baker & Simon Associates in association with Oregon Public Broadcasting. On PBS, Tuesday evenings, 9 to 30 November 1999.

The first episode, "The Tree of Life," explains how scientists, who were studying an unusual microbe that grows without oxygen in superheated sulfurous water off the Italian island of Volcano, unveiled an important clue about how all organisms are related to each other. The program draws an extended analogy between the arrangement of eight notes in a musical score and variations in the order of the four bases in a DNA strand to explain how comparative analysis of "special chains of bases" in all living organisms can inform us about the relative position of microbes, plants, and humans on the tree of life.

The idea that microbes are essential to recycling biomass and to maintaining the biosphere's chemistry is developed in the second program, "Keepers of the Biosphere." It begins with the mystery of Biosphere 2, the sealed, supposedly self-sustaining "micro-planet" built in the Arizona desert. Within a few months from the start of the "experiment," many species declined and disappeared and the oxygen levels in the man-made environment dropped well below 20%, possibly as a result of greater-than-expected oxygen consumption by microbes in the rich soil. These changes provide an entry into explanations of microbial roles in geochemical cycles and how very small things can affect very large things—such as climate. The scene then switches to the Sargasso Sea, where researchers discovered a gene that, they infer, comes from a previously unsuspected microbe, possibly one of the ocean's most abundant life forms. The search for the mystery microbe (represented by a cartoon man-in-the-moon head wearing dark glasses) among hundreds of identical-looking microbes is conceptually well-described with the aid of animations and exemplifies the excitement of the scientific hunt. We also learn that algae and bacteria produce 50% of the world's oxygen, that 100,000 microbes are present in a drop of water, and that all nutrient recycling is done by microbes as they use oxygen and release carbon dioxide. Nonetheless, this program is the least successful of the four at conveying its main message. It repeatedly states that our world could not exist without microbes, but its demonstrations of that claim require too many leaps of logic that fall short of the mark. Thus this segment is likely to be confusing to a general audience.

Because they focus on the practical aspects of microbes, the final two programs will be easiest for most viewers to grasp. "Dangerous Friends and Friendly Enemies" begins a discussion of infectious diseases by describing how humans usually live in peaceful coexistence with a microflora consisting of hundreds of species that inhabit our skin and our guts. These organisms actually maintain our health by keeping a small number of disease-causing microbes from becoming dominant. The program's metaphor of a dance explains that microbes and humans are engaged in a constant relationship of cause and effect much like the interaction between two experienced dance partners. But if an outside influence pushes the partners out of balance, hostile microbes can get the upper hand.

Computer bugs. The series uses computer graphics to help reveal the microbial landscape of the human body.

A recent outbreak of a deadly respiratory illness in the Four Corners area of the southwestern United States is discussed to show how the sudden appearance of an apparently new disease can be fostered by something as seemingly unrelated as a change in climate caused by El Niño. The story follows the steps taken by researchers and health organizations to identify new infectious agents (in this case, a hantavirus) and to track down environmental factors that may influence the development of new diseases.

The fourth segment, "Creators of the Future," focuses on microbes as benefactors, calling them "the most brilliant chemists on Earth": They produce most antibiotics, they genetically engineer disease-resistant plants, and they degrade pollutants. These practical roles of microbes are highlighted through filmed segments that take the viewer from a Douglas fir stand in Vancouver, Canada, to radioactive soil near Chernobyl.

Intimate Strangers succeeds admirably in showing that there is more to microbiology than germ busting. Parts of each episode will strike any microbiologist as not quite right, not quite accurate. But despite the occasional liberties taken in the telling, the series portrays the dominance and diversity of microbes as a group of invisible creatures on which all plant and animal life depends. It effectively conveys that microbes are Earth's most successful inhabitants; as the narrator reminds us, "the smallest microbes affect the biggest events."

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