

The ROI of Biotech

AFTER DECADES OF WORK AND BILLIONS OF DOLLARS, BIOTECH RETURNS CAN NOW BE SEEN.

In 19th Century England, the ideas of Charles Darwin and his friend Charles Babbage couldn't have seemed more unrelated. Darwin became a giant in biology for the theory of evolution described in his 1859 book, "On the Origin of Species." Babbage, whose efforts to build a digital calculator began in the 1830s, became known as the "father of computing."

Neither man would have imagined that, more than a century later, their pioneering efforts would combine to spark a radical technological sea change. But it's happening: biotechnology — an industry barely 30 years old — is now melding with information technology.

Investors in 2002 pumped about \$10 billion into the biotech industry across the board. Billions more are flowing in from the government as it responds to threats of bioterrorism. The return on these investments in human health and wellbeing promises to exceed the most hyped predictions.



“Biotechnology is a catalyst for new business growth and job creation,” says Jeff Mason, senior vice president at the Michigan Economic Development Corp. in Lansing, Mich. “New companies are continuing the momentum that has been created.”

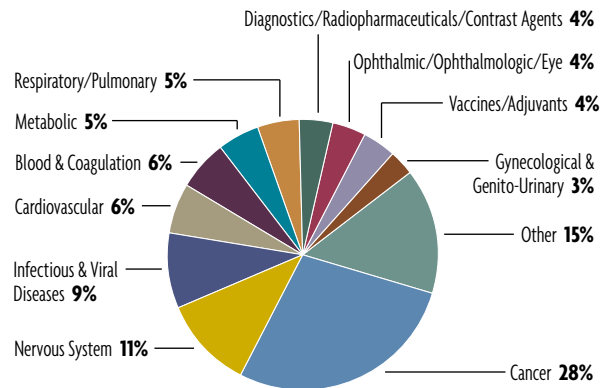
More Affordable Cures

The advances in computer technology have made tools that were once the province of big pharmaceutical companies affordable to small and midsize firms. Nearly 400 new biotechnology medicines that target ailments ranging from cancers and infections to autoimmune and neurological afflictions are in the drug development pipeline. “Now we’re playing on a level field,” says one biotech executive.

At the same time, the drug developers are fashioning diagnostic tests that can pinpoint diseases such as cancer earlier than any modern medical image. They also are developing tests that will allow physicians to predict whether a patient’s disease will respond to a particular drug and whether that drug will cause side effects. Other tests monitor treatments, so physicians can tell if the desired effect is being achieved.

Indeed, the recently far-out idea of “personalized medicine” — treatment based on a patient’s genetic makeup and particular disease — is fast becoming a reality, says Carol Kovac, head of IBM Life Sciences Solutions.

Where the R&D Dollars are Focused



Source: NDA Pipeline, Ernst & Young

amount of data that is accumulated and that can be used in the search for new drugs has grown exponentially,” says John P. McAlister, president and CEO of St. Louis-based Tripos.

Human Genome Impact

This has sharply accelerated the work of researchers trying to sift through the enormous amounts of new genetic data uncovered by decoding the genomes of humans and other organisms. The human genome alone consists of more than 10 billion base pairs of DNA. Contained in



Two people may have high blood pressure, but “your hypertension is not the same as my hypertension,” says George F. Schreiner, chief scientific officer of Scios.

IBM is hardly alone in its commitment to biotechnology. Other computer makers, including Sun Microsystems Inc., Hewlett-Packard Co. and Motorola Inc., also are chasing the genomic grail. Many software companies, from giants like Oracle Corp. to specialized firms like Tripos Inc., are writing programs to find molecules in the genomic data that could be turned into future drugs.

Such instrument makers as Agilent Technologies Inc., Affymetrix, Nanogen Inc. and Applied Biosystems are developing more efficient ways to test and screen candidate drugs. “The

this enormous mass of data is the genetic code for all human genes — the total of which could number as high as 100,000.

“Research is generating huge quantities of data from which scientists are trying to extract knowledge,” says Chris van Ingen, senior vice president of Agilent Life Sciences/Chemical Analysis, the Palo Alto-based unit of Agilent Technologies. “Identifying new drug targets is like finding a needle in the haystack, but more data does not always mean more needles. Sometimes it’s just more hay. We’re trying to remove as much

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hay as possible, without losing any data.”

Then there is the matter of understanding the role all the proteins coded for by those genes play in the body. “You can’t find genes without a roadmap, and the human genome sequence is just that,” says Charles Cantor, co-founder of the

scientists can improve diagnostic tests. The key, says Michael W. Hunkapiller, president of Applied Biosystems, a Foster City, Calif., unit of Applera Corp. of Norwalk, Conn., is “fail fast, fail cheap.”

With the help of high technology, that’s exactly what the biotech companies are doing. High



“The payoff promises to be enormous. Biotech is not just about money,” says G. Steven Burrill, CEO of Burrill & Company. “It’s about humanity, health and the preservation of the planet.”

government-sponsored Human Genome Project.

Before the human genome was deciphered, most searches for genes that contribute to diseases took years and eight out of 10 failed. The major pharmaceutical companies estimate that it costs them \$800 million to bring a new drug to market and takes almost 15 years. Glaxo Smith-Kline, for instance, says it spends \$450,000 per hour, 24 hours a day, to find new medicines.

Now, experts say, it is likely that the most important genes for all the major human diseases will be identified within the next two years. And while it might still take years before a treatment can reach the marketplace, once the gene is known,

throughput “labs on a chip” can screen 10,000 samples a day for activity against specific diseases. Instead of testing candidate drugs on live animals, their effects can be predicted by computer models. “The reliance on animal pharmacology is beginning to be replaced as we enter the molecular age,” says Michael Jackson, senior vice president of drug discovery at Johnson & Johnson, headquartered in New Brunswick, N.J.

Now in the Clinics

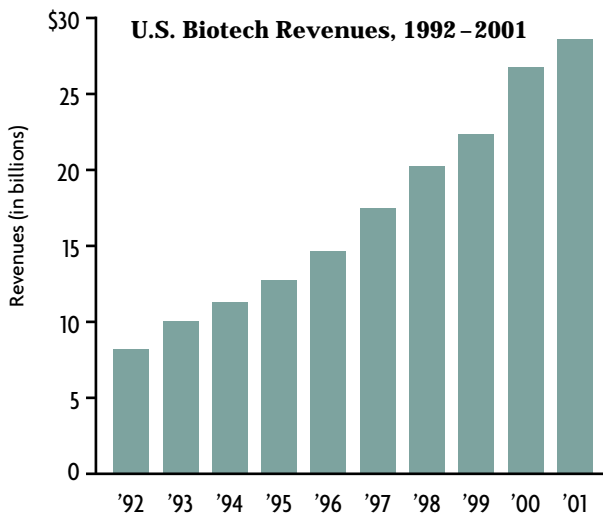
The first fruits of biotech’s next generation are beginning to appear in the clinic. Gleevec, a drug developed by Novartis AG in Basel, Switzerland, to treat cancer, and Herceptin, created by Genentech Inc. in South San Francisco, Calif., for breast cancer, are among the first to be based on the genetics of cancer cells. Both target specific proteins that cause the cells to stop proliferating. Unlike traditional chemotherapy, which works by killing off fast-growing cells, these drugs lack debilitating side effects.

Diagnostic tests based on genetics also are on the way. Urologists already are detecting bladder cancer with a urine test developed by Matritech Inc. Plus, the Newton, Mass.-based company is testing a simple blood test for breast cancer that may soon augment X-ray mammograms.

Moreover, drug developers are making drugs for smaller patient populations. In the past, drugs were developed to treat the largest number of people. Those that worked most of the time became billion-dollar blockbusters. But researchers are learning that, although millions of people may have the same symptoms, what looks like one disease is really many.

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A Growing Biotech Market



Source: Ernst & Young

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The Times – and the Labs – Certainly Have Changed

While much of the hand labor in the nation's manufacturing sector has been taken over by robots and advanced instrumentation, little has changed in pharmaceutical research laboratories since the 19th Century — until recently.

Over the years, hundreds of “wet chemists” have sat at the laboratory bench, surrounded by beakers and culture plates, combing through samples culled from nature. When a compound seemed promising, it was tested on hundreds of lab animals. Most tests were failures. When a new drug was discovered, bringing it to market took more than a decade and cost in excess of half a billion dollars.

No longer. In drug research labs these days, pixels are more prevalent than pipettes. Glowing monitors and carpeted floors occupy spaces once allocated to lab benches. Where candidate drugs used to be tested *in vitro* (in test tubes) and *in vivo* (in living organisms), the job now is done *in silico* (on computer chips).

Lab-on-a-Chip

Today, the drug game is played out in “laboratory-on-a-chip” tests: micro-assays and cassettes that can read thousand of samples in the time it would take a researcher to put a drop of sample on a microscope slide. “We can check out multiple drugs and structures before we ever pick up a test tube,” says George F. Schreiner, chief scientific officer at Scios Inc. “Ten years ago, you couldn't even think of doing that.”

The payoff will be highly targeted drugs that are safer and reach the market faster. They will cost less to develop, so consumers will pay less. And, analysts at PricewaterhouseCoopers predict that *in silico* technologies will shave two to three years off the drug discovery timeline as



well as cut the development cost by at least \$200 million.

In the not-too-distant future, drug targets may be identified, candidates screened to see if they are beneficial and harmless, and final compounds designed and tested on computer models — all before the first test is conducted on an animal or a human.

Driving the wave of change in biotechnology are the common interests of the drug developers and the computer and high-tech companies. Just when the computer companies were scouting out new markets, the wealth of data in the human

genome was deciphered.

In one fell swoop, the number of known human drug targets jumped from about 500 to more than 30,000. And that's just genes — add in the interactions of the myriad proteins resulting from that genetic coding and the number increases more than 10 times. “Genomic information is like a telephone book that's been scrambled,” says Alan Timmins, president and COO of AVI BioPharma in Portland, Ore. “All the information is there, but it's meaning is anything but obvious.”

Pharmacology is entering a new drug age, one in which compounds can be created with blazing speed and quickly turned to combat terrorism and biological warfare agents.

For example, when an Animal Rescue Center in Atlanta called AVI BioPharma to report that many of the cats in its facility were dying rapidly of a mysterious disease, AVI researchers surmised that the infections were Feline Calicivirus — a viral infection closely related to the Norwalk virus recently identified as the cause of over 1,000 infections on cruise ships. Within days, AVI created and delivered a small quantity of a drug that blocked the infectious disease. The animals treated with the drug survived. ■

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Two people may have high blood pressure, but “your hypertension is not the same as my hypertension,” says George F. Schreiner, chief scientific officer of Scios Inc., a drug development company in Sunnyvale, Calif. Hardening of the arteries, or atherosclerosis, is likely to turn out to be a family of 50 to 60 diseases, he predicts. “This is the first major advance in understanding disease since the heyday of the physiologists,” Schreiner says.

The fragmentation of diseases into smaller segments suits the biotechnology companies just fine. After all, the odds of coming up with a billion-dollar blockbuster are slim. And as a result of a wave of mergers and acquisitions in recent years, the number of big, deep-pocketed pharmaceutical companies with which to partner has fallen from about 30 to fewer than 10. But small and midsize biotech companies can find smaller niches — and they can make a tidy profit with a small sales force.



Faster Drug Approvals

Also, knowing early in the development process which patients will be helped will speed up the approval process. Human clinical trials to determine a drug's efficacy will proceed more rapidly and produce better results if the test subjects are selected from targeted populations. “Hundreds of experimental drugs for the treatment of cancer have failed FDA approval because, until now, it has not been possible to predict which patient will respond positively,” says Bailey E. Dotson, chief executive officer of CeMines, an Evergreen, Colo., startup focusing on a proprietary technique it calls “molecular fingerprinting” — the development of diagnostic tests for a range of cancers that match treatments to a patient's medical profile.

Genentech's Herceptin, for example, is effective only on breast cancers with a certain receptor, and that receptor is found only in about 30 percent of breast cancer patients. But on those patients, it is a highly effective treatment.

It is this combination of targeted drugs and di-

agnostics that is ushering in an era of personalized medicine. In the not-too-distant future, a fast analysis of a patient's DNA in a doctor's office will tell the physician which drug would be the best candidate for that patient's disease.

Major medical centers are pushing into what the computer industry likes to call “information-based medicine.” They are boosting their ability to predict outcomes for individual patients by computerizing all medical records. The Mayo Clinic, for one, has built a database of complete records — from medical images to medication history — of more than six million patients. “Personalized medicine isn't that far away,” says IBM's Kovac.

The dream of treating newborn babies for genetic diseases that wouldn't effect them until middle age, producing powerful medicines tailored to an individual patient or implanting healthy organs produced by a patient's own cells is still a long way off. But the blindingly fast push into a new era of medical treatment makes this eventual outcome more plausible. Some experts even believe that the productivity of biotechnology is now scaling like the computer industry.

Just as the ideas of Darwin and Babbage changed the world in the 19th Century, the convergence of their technological progeny is poised to make an indelible mark on the 21st Century. And the payoff promises to be enormous. Biotech is not just about money,” says G. Steven Burrill, CEO of Burrill & Company, a San Francisco-based life sciences merchant bank. “It's about humanity, health and the preservation of the planet.” Now *that's* one heck of an ROI. ■

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