As the economics of R&D evolve, the Salk and other private research institutes become increasingly crucial to health care's changing value chain.

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The New Arc Biomedical

by Lawrence M. Fisher

hitecture of Research

Photography by Vern Evans

Lawrence M. Fisher
(fisher_larry@bah.com), a contributing editor to *strategy+business*, has covered technology for the *New York Times* for more than 15 years and has written for dozens of other business publications. Mr. Fisher is based in San Francisco.

Perched on a cliff overlooking the Pacific Ocean at La Jolla, Calif., is the Salk Institute for Biological Studies, a singular facility dedicated to scientific research. Inside its two mirror-image towers, built of concrete, teak, lead, glass, and steel, more than 2,000 scientists have trained, and many have gone on to lead other prominent research centers around the world. Five Salk-bred scientists have won Nobel Prizes, and four current faculty members are Nobel laureates. They work in light-flooded laboratories that lack internal walls, which allows reconfiguration at will. But no amount of past experience compares with the grand rearrangement in which they are today engaged — the reshaping of the value chain for biomedical innovation.

On an innovation path that begins with a discovery in basic biology and ends with a new drug, independent research institutes play a role that is unusual, often unseen, and more crucial than ever. Labs like the Salk Institute, the Cold Spring Harbor Laboratory on Long Island, and the Whitehead Institute for Biomedical Research in Cambridge, Mass., are vital to a biotechnology industry increasingly in need of their support.

The twin threats of bioterrorism and new virulent diseases like severe acute respiratory syndrome (SARS) underscore the continuing need for innovative therapeutics. Yet despite a recent recovery in the shares of biotech companies, investors remain reluctant to fund basic research. With commercial entities concentrating on later-stage drug development efforts, the independent laboratories have a fresh mandate to pursue the basic science that leads to breakthrough drug discoveries.

"Bioterror — it's terrible that we have to deal with that, but in some ways it has catalyzed the new relationship between government and industry in medicine," says Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases, the arm of the National Institutes of Health (NIH) that focuses on diseases such as AIDS, hepatitis, and other viral and bacterial infections. "Successful partnering is one way of keeping up with these infectious microbes, to fill the gap between research and medicine. Nothing is more true than the need for a successful biotech industry to partner with government and academic institutions. There is no one group that can do it alone."

In some ways the biology world is seeing a return to an old model, one in which medical research was funded and directed by the National Institutes of Health, with academic institutions providing both the breakthrough insights and the tedious but essential bench work that makes science pay off. Increasingly, the Centers for Disease Control and Prevention (CDC) is also funding basic research in the United States, and government investment in biology has been growing across Europe and Asia for the past several years.

But today there is a new environment, with a new sense of urgency, particularly in the United States. Project BioShield, a proposal now before Congress, would increase the authority and flexibility of the NIH to expedite research and development of critical biomedical countermeasures against bioterror and untreatable infectious diseases, and would provide up to $8 billion in new funding. NIH and CDC officials say they are counting on an unprecedented level of collaboration among independent labs, academia, and industry to meet these challenges.

One of the first manifestations of this new three-way collaboration will be a massive database integration project intended to help public and private researchers share their findings more easily. In the long run, with or without Project BioShield, the NIH intends to foster more numerous and more profound shared research and development of new drugs.

Biotech in Check

Prior to the advent of biotechnology in the late 1970s, pharmaceutical innovation was largely a matter of serendipity coupled with varying degrees of refinement in the chemist's lab. To cite one ready example, aspirin, introduced by F. Bayer & Company in 1899, was a purified form of salicylic acid, derived from the bark of the willow tree. In the decades that followed its release, the large pharmaceutical companies — most of them other chemical companies, specifically, makers of textile dyes — developed vast libraries of other naturally derived chemical compounds that were tested on a broad array of diseases in hopes of finding a random "hit" that could be purified for use as a drug.

In the late 1970s, biotechnology turned the drug discovery paradigm on its head. Beginning with an understanding of key diseases at the molecular level, biotech companies sought to reproduce natural proteins and hormones (and variations of them) that could treat hitherto unmet medical needs. Early biotech drugs, such as human growth hormone and insulin, were replacement therapies, compensating for deficiencies in the body. More recently, the industry has developed innovative treatments for cancer, heart disease, and rheumatoid arthritis, using genetically engineered proteins and antibodies to intervene in the course of these illnesses.

Biotech also changed the way biomedical discovery was financed. Most early pharmaceutical research was funded and performed internally by companies. Government-financed research began in the late 19th century, with the founding of the NIH's predecessor, the Laboratory of Hygiene, in 1887, with an initial budget of $300. In 2002, the NIH had appropriations totaling nearly $23.4 billion, with 84 percent of its investment distributed among more than 2,000 research institutions throughout the nation and abroad. Philanthropic organizations, like the Rockefeller Foundation in the U.S. and the Wellcome Trust in the U.K., are also major funders of biological research.

Twenty-three years ago, the successful public offering of Genentech Inc., the world's first biotechnology company, appeared to pave the way to a new paradigm: the funding of basic research by the public equity markets. That wasn't the way the IPO was pitched, naturally; rather, investors were told that buying shares in Genentech, and cousin companies like Amgen, Biogen, and Chiron, was akin to buying the initial public offerings of IBM or Xerox. The marriage of molecular biology and medicine promised the creation of an entirely new growth industry, and with it, the kind of outsized return on investment that accompanies fundamental change.

But the practical significance of the first biotechnology wave seemed to be the establishment of a new relationship among business, academic institutions, and investors. The three parties, whose interests historically had not always coincided, appeared to have found a way to collaborate to advance and commercialize basic scientific research at speeds previously thought impossible. The founders of the early biotech companies included leading scientists from such schools as the University of California at San Francisco, the Massachusetts Institute of Technology, and Stanford University; driven both by dreams of Nobel Prizes and visions of wealth, they pursued basic research with a zeal unknown in the established pharmaceutical industry. Their failures were many, but their successes were profound: powerful new drugs for cancer (Chiron's Interleukin-2, Idec's Rituxan), heart disease (Genentech's Activase, Centocor's ReoPro), and a host of other ailments.

Although the biotechnology pioneers fulfilled much of their early promise, they did not, with a few notable exceptions, provide much of a return to investors. Indeed, the combined market capitalization of the entire biotech industry today is barely more than the sum of public and private dollars invested over the last three decades.

Not surprisingly, venture capitalists and public equity investors alike have grown wary of investing in early-stage biotech concerns, no matter how promising their premise or how many stellar scientists they employ. The markets are interested in products and in companies with a near-term prospect of profitability. Pure innovation — research without the potential for immediate commercialization — has little luster. Today, after a peak of excitement fueled by the Human Genome Project, valuations of biotech companies are down. With dollars flowing only to later-stage ventures, most biotech companies have cut back or eliminated their own investment in basic research. And the large pharmaceutical companies, consumed by a wave of consolidation and driven by the financial markets to develop "blockbuster" drugs, have not been inclined to finance innovative biomedical research.

These developments would be tragic, for medicine and humankind, were it not for the thousands of research scientists plugging away in their labs in academia — and independent institutes like the Salk.

Independent Virtues

In many ways, there is little difference between a lab at Stanford and a lab at the Salk Institute. But the independent research institutes have some attributes that make them particularly apt partners for the biopharmaceutical industry. Basic research thrives at these institutions, at least in part because they do not answer to shareholders or university regents, who often have multiple agendas (providing undergraduate education, creating jobs, and pleasing political constituencies) that have little to do with innovation.

More fundamentally, the independent labs offer an inviting environment for the best and brightest scientific minds. These are collegial places, typically home to one or more "stars" of the biology world, like James Watson and Francis Crick, co-discoverers of the structure of DNA, who reside at Cold Spring Harbor Laboratory and the Salk, respectively. These institutions provide an open campus, where professors and post-doctoral students alike share cafeteria tables with Nobel Prize winners. There is minimal bureaucracy, so decisions can be made fast. There is an open exchange with other labs, universities, and the corporate world. Scientists are not required to teach, and they have the freedom and time to focus on the work that interests them most. Without the administrative duties, undergraduates to teach, and campus politics typically found in university settings, scientists spend nearly all their time doing science.

"Our people devote 100 percent of their time to problem- and curiosity-driven research," says Richard Murphy, president and CEO of the Salk. "We don't teach very much; they don't have a lot of administration to do. We have an environment where faculty members and their students spend all of their time doing research, which means it's very efficient."

The Salk Institute for Biological Studies was established in 1962 by Jonas Salk, the developer of the polio vaccine. Given the fear engendered by polio in the first half of the 20th century, Jonas Salk's creation of the first effective vaccine made him an international hero. He never patented the vaccine, nor did he earn any money from his discovery, preferring to see it distributed as widely as possible. But he dreamed of creating an independent research center where a community of scholars interested in different aspects of biology — the study of life — could come together to follow their curiosity.

For more than a year, Dr. Salk toured the country in search of the right location for his research center. Finally, wooed by San Diego Mayor Charles Dail, who had had polio, he was drawn to 27 acres on a mesa in La Jolla, just west of the proposed site for the new University of California campus then planned for San Diego. With a gift of the land from the citizens of San Diego and with initial financial support from the March of Dimes Birth Defects Foundation, Jonas Salk, who died at age 80 in 1995, was able to build the institute.

In Jonas Salk's original vision, biologists, sociologists, artists, and other luminaries would work together in a collaborative environment to explore questions about the basic principles of life and consider the wider implications of their discoveries for the future of humanity. Working closely with architect Louis Kahn, he summarized his aesthetic objectives by telling the architect to "create a facility worthy of a visit by Picasso."

The artists and philosophers have long gone elsewhere, a part of the original vision that did not survive. But the stark concrete edifice at the edge of the sea still provides a striking home to a small cadre of brilliant scientists. The Salk Institute is renowned for its work in three areas: molecular biology and genetics, the neurosciences, and plant biology. The institute has 56 faculty and about 250 post-doctoral students, and although it offers no degree programs of its own, the Salk also hosts 100 graduate students from the nearby University of California at San Diego.

The difference between the Salk and a great research university is a matter of focus and freedom, says Dr.

"A successful biotech industry needs to partner with government and academic institutions," says a senior NIH official. "No one group can do it alone."

Murphy, who joined the institute in October 2000. "A university department has to have a broad range of course offerings to cover its teaching responsibilities, and so they have to hire people for that," he says. "We just choose the very best people we can find. People here have the time to really focus on the fundamental questions.

"The faculty have absolute freedom to do what they want. If we hire a neuroscientist, and a week later, he says there's an interesting problem in cancer he wants to pursue, we say Godspeed," he says. "We give them the freedom to do it."

Any scientific specialty reaches a point where the world becomes a very small place, and most of its practitioners know one another from conferences and global symposia. Ask any scientist at the Salk how he or she came to be there and the usual response is recruitment by a friend or a peer. And despite the generous freedoms offered by the institute, staying in this club has the same requirements as joining: a steady stream of publications in peer-reviewed journals, winning grant proposals from the National Institutes of Health, and the kind of advisory board appointments that help anoint a professional as "preeminent" in his or her field.

But managing 56 "legends in their own minds," as one faculty member jokingly calls his colleagues, can be a challenge. Scientists who join the Salk Institute — all have had distinguished careers elsewhere — have made a conscious decision not to join industry and not to teach, but to pursue science in an environment where they are not distracted by classroom duties or shareholders. They tend to do just what they please. They answer to peer review, not performance appraisals.

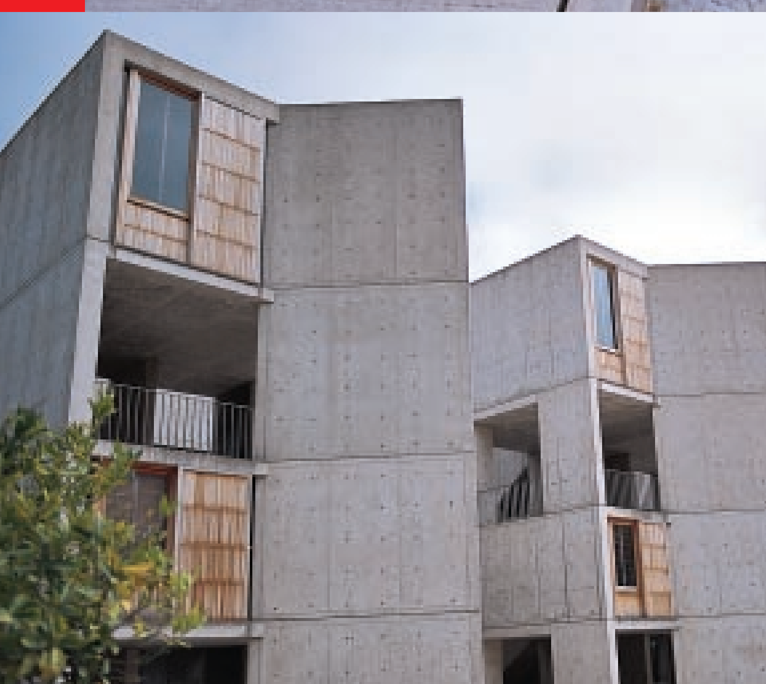
Although several Salk Institute scientists have helped start companies, very few have left the institute to work in the commercial world. "I was offered a big job in industry, and attractive as that seemed, it became clear I would be responsible to the president, who was responsible to the shareholders, and that my goals, which were driven by intellectual curiosity, were unimportant," says Geoff Wahl, a professor in the Salk gene expression lab, where he and his colleagues pursue the molecular biology of cancer.

He rejected the offer. "Freedom has no amount of monetary consideration," he says.

Similarly, Inder Verma, a Salk professor also specializing in cancer research, says, "Within 10 minutes of receiving an offer or inquiry, I send a letter saying, 'I'm flattered, but I have no thought of leaving.'" At the Salk, he says, "The science has gone well, it's a very nice place to live, and I have a very substantial influence in the institute, how it's run and how it's evolved. That doesn't mean I always get my way, but I have an influence, I feel welcome. I have an opinion that counts."

Facing the Market

Of course, no freedom is absolute. The trustees at the Salk and other such institutes recognize that they have a responsibility to society to deliver advances in medicine that will improve people's lives. Moreover, foundations and individual donors today seek returns on their philanthropic investments: In a world whose troubles are as apparent as its opportunities, they want to see their contributions made manifest in their lifetimes. That means channeling scientists' enthusiasms to the real-world applications of their research, and encouraging them to file for patent protection and think about licensing opportunities. In some cases a subtle pressure is applied, but scientists who have seen peers start companies or devel-



op breakthrough drugs are increasingly taking the initiative in seeking applied solutions based on their work.

"A number of years ago, 18 or so, there was not a great deal of interest on the part of scientists here in biotech startups or commercializing their discoveries," says G. Morgan Browne, chief financial officer of the Cold Spring Harbor Laboratory. "That certainly has changed."

In the early years, scientists at Cold Spring questioned whether it was appropriate for institutions to make money on discoveries made via public money. To mollify them, the Cold Spring board created a science fund to plow the royalties back into research.

The science fund "acts as a sort of endowment at the laboratory, and each year our revenues go back into funding science," says Mr. Browne. "That changed the thinking of a lot of our scientists, who have become really quite active in the area. Today there are about 15 biotech companies, more than half of them public, founded in part or in whole on science done here. Our policy was always that we didn't invest any money in these startups, but we were willing to exchange intellectual property for equity, from 1 or 2 percent up to 35 percent. This has built a nice chunk of money in our science fund — $20 or $30 million."

Licensing revenues help offset the decline in philanthropy that has accompanied the long slump in the U.S. economy. Although corporate spending has remained roughly constant, and NIH funding has actually increased in recent years (and will increase further if the BioShield bill passes), donations have fallen significantly.

"Funding from foundations has been seriously affected, and that applies to private individuals as well," Mr. Browne says. "The days when we got small blocks of shares as year-end gifts, those are over."

One way the Salk has balanced freedom and responsibility is by making all salaries dependent on so-called soft money, funding that is attached to specific research grants, typically from the NIH. The Salk receives about 66 percent of its funding from NIH grants, with the balance coming from philanthropy, private funding agencies like the American Cancer Society, and an endowment. Scientists are responsible for raising the money that pays their own salaries and funds the research in their particular labs.

"It's a lot of pressure," says Dr. Murphy. "We do supplement their incomes above the level NIH sets, and nobody has ever been fired for not bringing in their own salary. But it keeps people lean and hungry."

Historically, income from Salk Institute discoveries licensed to biotech or pharmaceutical companies has been a small part of the revenue mix, but in today's climate there is pressure to rebalance the ratio, because this money can be used for administration, equipment, and sundry other expenses explicitly not covered by grants.

In a scholarly culture that prizes independence and intellectual purity, the management challenge in goading scientists toward an increased market focus is profound. Polly Murphy, director of the Salk's Office of Technology Management (and no relation to Richard Murphy), likens it to "the worst nightmare of a biotech company," where the scientists get the chance to tell investors and management, "We don't care what the market is, we work on what we want to work on.'"

Underlying the enhanced commercial focus at the private institutes is the Patent and Trademark Law Amendments Act, more commonly known as the Bayh-Dole Act. Passed by Congress in 1980, Bayh-Dole gave universities and nonprofit institutions control of the inventions that arise from research supported by federal funding, providing the basis for current technology transfer practices at the Salk and elsewhere.

Prior to Bayh-Dole, the transfer of new technologies from universities to corporations was a haphazard, low-priority function at most schools. But in the past two decades, the independent labs and universities each have become far more assertive and entrepreneurial in marketing their discoveries. Stanford University, long considered a leader in promoting and profiting from its intellectual property, earned more than $52 million in royalties in 2002.

Technology management at the Salk Institute has resulted in more than 350 U.S. patents and more than 250 license agreements with pharmaceutical, biotechnology, and reagent supply companies. In addition, 17 startup companies have been founded to develop the Salk's technology, most notably Ligand Pharmaceuticals Inc. and Neurocrine Biosciences Inc., both based in San Diego. Ligand currently produces drugs for cancer, chronic pain, and skin disorders. Neurocrine is a neuroscience company focused on the discovery and development of novel therapeutics for neuropsychiatric, neuroinflammatory, and neurodegenerative diseases and disorders.

One drug that came directly from research at the Salk is Ligand's Panretin, a topical treatment for AIDS-related Kaposi's sarcoma that works by binding to and activating receptors inside a cell. Ronald M. Evans

Panretin, a treatment for AIDS-related Kaposi's sarcoma that works by binding to and activating receptors inside a cell, came directly from Salk research.

cloned the first nuclear receptors, including the retinoic acid receptors ultimately used in Panretin, at the Salk in the mid-1980s. Ligand, originally known as Progenx, incorporated in 1988 and obtained an exclusive license to Dr. Evans's work on these receptors. Clinical trials for Panretin began in the mid-'90s; in May 1998 Ligand requested marketing approval from the FDA for the drug, and it was granted later that year.

The Salk encourages its scientists to think about commercial applications of their work in various ways, from lunches with staff patent attorneys — featuring notably better food than the cafeteria serves — to Dr. Polly Murphy stalking the labs asking researchers what they've invented lately. The institute is quick to patent discoveries that may lead to drugs and is not shy about marketing its intellectual property to potential licensees. But it is always a delicate balancing act.

"If an invention comes out of a lab, and it is a patentable invention we feel may have commercial viability, we will always file the patent," says Dr. Polly Murphy. "But pricing is really tricky. You can't model it. It's hocus-pocus. Part of it is gut, experience, it's what we've gotten in the past. Because of my background, I know how the other side is going to react. I'm not going to ask for an 8 percent royalty because I'm not going to get it, but 2 to 3 percent they may go for." Ask too high a price and the invention will not be picked up by industry; too low a price and the Salk will not be adequately compensated.

Other "university and tech transfer offices have taken a beating in the last two years for getting too greedy," says Dr. Polly Murphy. "I don't have a provost saying to me, 'We expect you to bring in so much money to fund the research.' We get things done because we try really hard to be flexible; we'll take royalties, cash, stock, whatever. I can be flexible because I don't have a specific income requirement. The goal is to get these products out there where they can be useful, to help a human."

Currently, the Salk's biggest moneymaker is an HIV-related antibody that it sells to diagnostics companies, bringing in $700,000 to $800,000 annually. In total, the institute's Office of Technology Management generally brings in $3 million to $5 million in revenues, with 30 to 40 percent paid to the faculty members, and some to their labs. Patent expenses take another chunk. Net is $1 million to $2 million, Dr. Polly Murphy says.

"If you look at tech transfer offices, something like 80 percent do not make money," she says, noting that this is equally true of university and independent labs. "There's a perception by management that they all make a lot of money. My management understands that we don't have a golden egg. It's okay to break even. Because if we break even and serve the faculty and society, then we won."

New Partnerships

It's likely there will be more wins at the research institutes in coming decades, as the four forces driving biomedical research and development — industry, government, finance, and academia — evolve the ways they collaborate.

The partnership between biology research and private equity investors is perhaps the most intricate and variable. This is unsurprising since it is a fairly recent phenomenon, dating to a 1976 meeting of Robert A. Swanson, a venture capitalist with the Silicon Valley firm Kleiner Perkins Caufield & Byers, and Herbert W.

Boyer, a biochemist at the University of California at San Francisco. In the early 1970s, Dr. Boyer and Stanley Cohen, a geneticist at Stanford, had pioneered a new scientific field called recombinant DNA technology. Excited by the commercial potential of this scientific breakthrough, which he'd read about in a journal, Mr. Swanson called Dr. Boyer and requested a meeting. Dr. Boyer agreed to give him 10 minutes of his time. The meeting extended from 10 minutes to three hours over beers; by its conclusion, Genentech was born.

Mr. Swanson and Dr. Boyer faced skepticism from both the academic and business communities, but within a few short years, they had invented an entirely new industry. In the decades that followed, venture capitalists partnered with scientists to forge new companies from the research laboratories of leading universities and independent institutes all across the United States. (Lacking a well-developed venture capital industry, Europe and the rest of the world lagged behind, but by the 1990s, the model developed in the U.S. had been replicated in the United Kingdom, France, Germany, and Israel.)

For many years, venture capitalists were a common sight at research institutes, walking the halls in search of the next hot biopharmaceutical startup, much as they staked out Stanford for dot-com opportunities. When the biotech bubble burst in late 2000, the venture capitalists disappeared, and with the prolonged slump in biotech shares, they have stayed away.

But in 2003, new drug approvals, including Genentech's Xolair for asthma, Biogen's Amevive for chronic psoriasis, and Gilead Sciences' Hepsera for hepatitis B, prompted a mini-rally in biotech stocks. Although most venture capitalists are still looking for later-stage investments, some say they are revisiting the labs. "We're back in these institutes," says Dennis Purcell, senior managing partner of the $400 million Perseus-Soros BioPharmaceutical Fund.

The labs, for their part, are adding drug development skills, moving new molecules farther along the road from lab to clinic. In part, they are taking more control of their discoveries' futures, making sure they are developed properly. But they are also hoping to claim more of that later-stage capital, or to reap a bigger reward from pharmaceutical partners. "Among my partners, as we look at the academic institutes, they're getting later and later stage," Mr. Purcell says. "They may not have all the infrastructure of a company, but you can certainly buy things out of the institutes at a much later stage than you could 30 years ago."

To some extent, the institutes are simply responding to market forces. If the market undervalues basic science, as it has in recent years, the labs can move in the direction of more applied research. But whether that move will result in more successful biotech startups, or in more innovative drugs' reaching the market, remains open to question.

"There's extreme pressure today for academic institutions to be major contributors to economic growth," says G. Steven Burrill, chief executive officer of Burrill & Company, a San Francisco-based life sciences merchant bank. "That didn't used to be part of their brief; they were there to win Nobel Prizes. But there's still a big gap between a science project and a company. We have an awful lot of biotechs that are science projects disguised as a company."

The skills gap between academic institutions and large pharmaceutical companies means the two would be natural partners in the increasingly collaborative biomedical world. But this partnership, too, is evolving. The larger companies are often reluctant to look at very early stage discoveries, so they sometimes wait until a biotech company has at least partially validated a potential drug before getting involved. Typically a biotech company charges a substantially higher licensing fee than an institute would, but some of the risk has been removed.

"It's often very difficult to get a pharma company interested at such an early stage," says Thomas Ittelson, director of intellectual property at the Whitehead Institute for Biomedical Research in Cambridge, Mass. "Often they want a biotech company to vet it first. I've done deals with Lilly, Pfizer, Merck, but it's easier with smaller companies. Ultimately, though, it's the Pfizers and Mercks that will take these things forward."

There is "a symbiotic relationship between early pharma development and what we can do at Whitehead," Dr. Ittelson says. "I can license some discovery to a pharma company, and on top of that get a couple of million in sponsored research at Whitehead. We may discover a new fatty acid that potentially controls whether the body uses fat, but unless some company takes that raw scientific discovery and spends a lot of time, money, and expertise developing it, it will never become a therapeutic or something that will help mankind's health and happiness. We may make a discovery, but it's not going to turn into a drug unless somebody puts $200 million and a lot of time into development work. That's not what academia can do."

The Whitehead, founded in 1984, is an independent research institute whose 13 senior faculty members all have professorial appointments in the biology department of the Massachusetts Institute of Technology.

"One of the things we are pushing at Whitehead, even more so than at MIT, is to combine basic discovery work here appropriately with pharmaceutical development," Dr. Ittelson says. "Some of our big successes have actually been licensing discoveries to companies, and doing joint development, where they move forward on drug development and we move forward on trying to understand the biology. We get an interest in the drug, and I can also get some nice funding. The professor might do some consulting, and he's got some new money in his lab that he doesn't have to beg from the NIH."

The Art of Technology Transfer

One challenge to forming collaborations is that the typical invention at a research institute is pretty intangible. Technology transfer officers struggle to assign a value to an insight, and sometimes to persuade the owner of that insight to share it.

"Our technologies tend to be very early stage, and it's very difficult to separate the technology from the individual early on," says Kathleen A. Denis, director of technology transfer at Rockefeller University in New York. "If the individual doesn't want to participate, it's not going to go well. I don't have a widget to sell."

So part of the technology transfer director's job is missionary work, talking to scientists one on one. "There's nothing I can do, or want to do, to force them to show me something. But I can say, 'We have a nice place in society, a nice piece of ground, no taxes, bags of money from NIH and donors; and they're all sort of expecting something in return,'" Dr. Denis says. "'If we had something of benefit to humanity, why wouldn't we want to give something back?' and a lot of people fall for that. It's not for the money, although if we do it well, there will be some financial gain. We really do have a very privileged place in society."

Dr. Denis says she does not push too far. "It's hard to be terrifically assertive," she says. "The best contacts come from the individual scientists themselves. You not only have to convince your own scientists this is something they want to do, you have to convince the scientists and businesspeople at company X. If the scientists get along, we businesspeople follow. It's just details after that. We don't have a finished product, and the company has to make a substantial investment to take it forward. That's a lot easier if there's a mutual respect."

One aspect of partnering with independent labs that is difficult for many established companies is maintaining a generous information exchange and publication policy. Paul Herrling, head of corporate research at Novartis in Basel, Switzerland, says this is crucial. "In a science culture, you only get information if you give information. My view is it pays a lot to be liberal. You always get more back than you give because the rest of the scientific community is much bigger than you. Scientists will talk anyway, so you might as well leverage it and get something in return."

Scientists at the independent laboratories are accustomed to talking frequently and candidly with their colleagues and competitors at other institutions around the world. Much of this communication is informal, and is an integral part of a culture where the goal has always been publications, not profits. Now, NIH leaders say they would like to formalize that exchange of ideas to better align research efforts in academia, independent

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labs, industry, and government.

“If you look at the distribution of academic and research institutes, these centers of excellence, it maps very well to NCI’s map of cancer centers,” says Andrew C. von Eschenbach, director of the National Cancer Institute. “There’s a very significant alignment of basic research and our strategic initiative. We have to devote adequate resources so [the cancer centers and independent institutes] don’t get an unfunded mandate. We also have to provide a bioinformatics infrastructure.

“In return for that, there has to be better horizontal integration between them,” he says. “We’re providing more resources; in return, they have to give back to the community.”

Dr. von Eschenbach has set the NCI a challenge goal to eliminate the suffering and death due to cancer by 2015, and he is counting on the collaboration of the independent research institutes. “This is not a goal to eliminate cancer, although that may happen someday, but we may have enough knowledge to eliminate the burden of the disease,” he says. “It will only come about with a seamless interaction between government, industry, and academia.”

Back at the Salk, collaboration is simply a way of life. Indeed, the very structure of the labs — and certainly the culture created by Jonas Salk and nurtured over the years — was designed to facilitate collaboration within the institute.

Over the past year, publications by Salk faculty have highlighted discoveries in cancer, AIDS/HIV, Alzheimer’s disease, Lou Gehrig’s disease, and other critical illnesses. Sydney Brenner, a distinguished member of the Salk faculty, shared the Nobel Prize with John E. Sulston from Cambridge University in the United Kingdom and H. Robert Horvitz from MIT for their contributions toward discoveries about how genes regulate organ growth and the process of programmed cell death. And Dr. Evans shared two major prizes with Pierre Chambon, honorary director of the Institut de Génétique et de Biologie Moléculaire et Cellulaire in Strasbourg, France, for their work in discovering nuclear hormone receptors, revealing their structure and function, and defining their central role in human physiology.

“The quality of science here at the Salk is spectacular, and the environment is wonderful,” says Dr. Richard Murphy. “Every Friday afternoon, we have a faculty lunch, with sandwiches. The guy who would never miss that is Francis Crick, at 86 years old, and Brenner is the same way. These guys have the ability to ask the big questions.” +

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Resources

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The Salk Institute for Biological Studies: www.salk.edu

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