TECHNOLOGY TRANSFER

UC Goes Where Harvard Feared to Tread

Call it a sign of the times. In 1980, a plan to start a company at Harvard to commercialize university inventions collapsed when faculty members claimed it would erode academic independence and raise potential conflicts of interest. Last week, the University of California (UC) announced plans to set up a similar company, but nary a protest was heard. The difference? A decade of growing university-industry links has made the idea seem less threatening—and UC, which is feeling the chill of California's recession, needs extra income.

"We're going to try hard to protect what the faculty is already doing."

–Ronald Brady

The proposal UC officials presented to the university's Board of Regents last week calls for launching a for-profit company to help UC turn more of its patents into products—and cash. Those behind the plan believe there is a lot of untapped potential: Only about 25% of UC patents are actually licensed by companies, although at least another 25% are believed to have commercial possibilities. The proposed company, to be called the UC Technology Development Co., would try to take those undeveloped technologies a step toward commercial application either by giving UC researchers money to do additional development themselves or by spinning off a startup company to do the work. After that, it would try to attract an industrial investor.

UC Technology Development would have first refusal rights to fund further development of any promising—but not yet marketable—technology coming from the UC campuses or the three national laboratories that UC manages for the Department of Energy: Los Alamos, Lawrence Livermore, and Lawrence Berkeley. It would then get exclusive rights to form a company around the technology or to license it, while retaining a share of the company or royalties. Profits from the venture would be reinvested, rather than going back into university research. A companion nonprofit corporation known as the UC Technology Development Foundation would take care of the actual patenting and licensing work.

UC officials project that the for-profit company will directly invest more than $65 million in an estimated 350 technologies between 1994 and 2001. Initial funding would come from the $27 million in licensing royalties that UC is already collecting, a quarter of which it now turns over to the state. (UC has asked the governor of California to let it keep all the royalties to support the new company.) In addition, the university hopes to raise another $370 million from venture capitalists and stock offerings. In return, California would eventually reap a big tax harvest if UC's projections are correct: The university claims that new companies spawned by UC patents—as many as six startups a year—could generate as much as $9.5 billion worth of "economic activity" by 2001.

When Harvard floated a similar idea a decade ago, it was shot down in flames after the faculty worried that commercial incentives would skew university priorities toward projects most likely to make money, rather than those that are scientifically the most interesting. California has often taken a more relaxed view, however. Startup companies spun out of Stanford's computer research laboratories spawned Silicon Valley, and California's biotech revolution got its start in academic labs. After 2 years of discussion with the UC faculty, says Ronald Brady, the university's senior vice president for administration, the concept of a technology development company no longer seems heretical. The possibility that company funding may tilt the academic playing field "is a legitimate concern," Brady says, "but we've told them that we're going to try hard to protect what the faculty is already doing." To help keep academic concerns at a minimum, the new company's board of directors will include one or two members of the academic council.

The proposal will face its first test when the new California budget request comes out in January. That will reveal whether the governor is willing to give up the state's share of the UC royalty income. The board of regents, which will meet again in March, will have the final say. But given the woeful state of the California economy, any proposal to wring more dollars from UC research seems likely to find a receptive audience. As one researcher involved in the ill-fated Harvard venture puts it, "The way people look at these things changes a lot with the economic situation."

–Christopher Anderson

SMOKING AND HEALTH

Signs of Damage by Radicals

Over the past few years, a growing band of researchers have pointed to free radicals as major culprits in health problems ranging from cancer to heart disease and even aging. And, since cigarette smoke contains a cocktail of free radicals—highly reactive chemical species with one or more unpaired electrons that oxidize many biological molecules including DNA—there's been growing speculation that the increased cancer risk faced by smokers may in large part be due to the insidious effect of these agents. A handful of in vitro experiments have lent support to this speculation by showing that tobacco smoke can oxidize isolated DNA. But there's been no hard evidence from human studies that smoking adds significantly to the oxidative assault that everyone's genetic material faces from the free radicals generated as a by-product of normal metabolism—until now.

Researchers from Copenhagen University, Århus University, and the Danish Cancer Registry report in the December issue of *Carcinogenesis* that they have found that the urine of smokers contains larger quantities of a tell-tale indicator of DNA oxidation than that of nonsmokers. From a public health standpoint, these results could be a mixed blessing: The Danish researchers who carried out the study are now trying to determine whether giving smokers large doses of antioxidants can reduce the signs of oxidative damage. But they worry that die-hard smokers may erroneously believe that such measures can make smoking safe.

The Danish group studied DNA oxidation indirectly, by recording the concentration of a compound called 8-hydroxydeoxyguanosine (8OHdG), which is released when enzymes called exonucleases repair oxidized DNA, in urine from a random sample of 83 Danish adults. They found that the 30 smokers in the sample excreted half as much 8OHdG again as did the nonsmokers, indicating that smoking greatly increases the rate at which DNA is oxidized. This could be caused directly by the free radicals present in cigarette smoke. But Copenhagen University pharmacologist Steffen Loft, a member of the Danish team, believes that the fact that smokers' metabolic rates are typically 10% to 15% higher than those of nonsmokers also plays a role. He suspects that the higher rate of cellular respiration in smokers is largely due to the enhancement of one particular metabolic pathway that results in the formation of free radicals.

In spite of the growing interest in free radicals, most researchers investigating the mechanisms by which smoking causes cancer have, until now, concentrated on the binding to DNA of the polyaromatic hydrocarbons found in tobacco smoke. More work must be done before it's possible to estimate the relative importance of the two processes in causing cancer among smokers. But Loft believes that DNA oxidation will prove "at least as important as aromatic binding."

The precise mechanisms by which smoking oxidizes DNA may be fascinating to pharmacologists. But for the broader cancer research community, the new results raise an interesting question: Can antioxidants such as vitamin C or beta-carotene reduce the risk of developing cancer? "I think most people in the field now feel we need some really big intervention studies" to test that idea, says molecular biologist Bruce Ames of the University of California, Berkeley.

The Danish researchers, in fact, have already taken a small step in that direction. They recently launched a study in collaboration with researchers from the Netherlands Organization for Applied Scientific Research's Toxicology and Nutrition Institute in Zeist to see if 8OHdG excretion can be reduced among smokers given high doses of beta-carotene. The point of the trial isn't to see if smoking can be made safer. Smokers are simply a good population in which to study the role of antioxidants in reducing DNA damage because of the high rate at which their genetic material is oxidized, explains Copenhagen University pharmacologist Henrik Poulsen.

The early signs are promising. Geert van Poppel and his Zeist colleagues have a paper in this month's *British Journal of Cancer* showing that the formation of micronuclei—fragments of genetic material left in the cytoplasm after faulty cell division—is reduced by about 30% in lung epithelial cells coughed up by smokers given 20 mg a day of beta-carotene (about six times the average daily consumption) over 14 weeks.

To epidemiologist Richard Peto with the Imperial Cancer Research Fund in Oxford, however, there's a serious downside to this wave of enthusiasm for antioxidants as potential preventative agents in the war against cancer. He fears that smokers will be lulled into a false sense of security, thinking that they can ward off tumors by dosing up on antioxidants. Tobacco smoke is "an absolute zoo" of noxious chemical species, notes Peto, and it's far too early to say that DNA oxidation by free radicals is the single most important factor underlying the high rate of cancer among smokers. Poulsen agrees. Even if the 8OHdG data suggest that DNA oxidation can be reduced in smokers, he says, the message will still be that the only sure way for smokers to reduce their cancer risk is to quit. But if the Danish-Dutch trial does produce positive results, and you're unavoidably exposed to free radicals—such as a city dweller inhaling automobile emissions all day long—it may well be worth taking a close look at your daily intake of antioxidants.

–Cláudio Csillag and Peter Aldhous

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SPANISH SCIENCE

Spain's Ambitions in Biology Threatened by Funding Freeze

MADRID AND BARCELONA—Ask Europe's leading molecular biologists where the continent's brightest young researchers in their field have been emerging from in recent years, and one answer that is given frequently may come as a surprise. "The Spaniards I've seen are exceptionally good," says Cambridge University protein engineer Alan Fersht, who wishes the current crop of British postdocs could match the creativity and productivity of their Spanish counterparts. Policy makers are similarly impressed. "Spain has made tremendous progress over the past 10 years," says Jean-François Stuyck-Taillandier, head of international relations at the French Centre National de la Recherche Scientifique (CNRS). So much so, in fact, that Spain is now CNRS's fourth leading source of international partners—eclipsed only by the United States, Britain, and Germany.

JORGE MARTIN

Too few jobs. "We have a lot of people abroad who can't come back."—Federico Mayor Jr.

By any standard, Spanish science has undergone a renaissance in the past decade. Until the early 1980s, Spanish researchers who wanted to make their mark internationally had little choice but to go abroad. But today, institutes like the Center for Molecular Biology (CBM) in Madrid are established features on the scientific map of the world, thanks in large part to a trebling of government research spending in the 10 years since Spain's Socialist party came to power. Although most disciplines have benefited from this expansion, the biggest explosion of scientific output has been in the biological sciences (see charts).

But behind all the good news is a nagging question: Will the final push needed to consolidate Spain's position as a scientific power materialize? To answer that question, *Science* made a week-long visit to Spain during the fall. What emerged from conversations with many of the country's leading biologists was unanimous acclaim for their government's past efforts—but coupled with a fear that Spain is losing the political will to invest in science. The world recession has hit Spain's fragile economy hard, forcing the government to spend marginally less on science this year than it did in 1991. Worse, say the country's top biologists, the prospects for young postdocs—the very people who've earned the praise of researchers like Fersht—will be dismal unless the funding momentum is maintained and the academic system is overhauled.

Spain now has "the critical mass to do first-class science," says molecular virologist Mariano Esteban, who's just been lured back from the State University of New York's Brooklyn Health Science Center to head the new National Center for Biotechnology in Madrid. And among established Spanish researchers, there's a level of satisfaction with government funding that would turn most U.S. biologists green with envy. "In general, we have no problems getting grants for projects," says immunologist Jordi Vives, from Barcelona's Hospital Clínic. But it's a different story for the legions of young Spanish biologists who don't yet have their own labs.

An important part of the Spanish government's effort to strengthen its scientific community has been a drive to send postdocs to work in the best labs in Europe and the United States. "It has been very easy to go abroad," says Federico Mayor Jr., a neurobiochemist at CBM. "[But] now we have a lot of people abroad who can't come back." The reason? Too few jobs. "I have not been in Spain for the last 7 years, except for vacations," says immunologist José Alberto Garcia. In 1991, he applied for a post at the Basel Institute for Immunology, and for a postdoc fellowship in Madrid. Although his proposal was good enough for the world-famous Basel Institute, it didn't make the grade in the scramble for jobs in Spain.

Even those who have managed to land a postdoc position in a Spanish lab face an uncertain future. Spain's biology labs have been churning out new Ph.D.s over the past decade, but the number of permanent jobs has failed to keep pace with the demand. And, to compound the problem, there's no equivalent of the U.S. assistant professorship—the key position that constitutes the