

Spain's Ambitions in Biology Threatened by Funding Freeze

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

Cláudio Csillag is a science writer based in Copenhagen.

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.

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

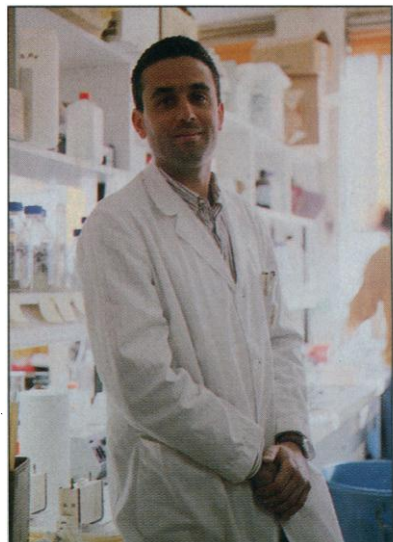
in 1991. Worse, say the country's top biologists, the prospects for young postdocs—the very people who've earned the praise of researchers like Fersht—will be dismal unless the funding momentum is maintained and the academic system is overhauled.

Spain now has "the critical mass to do first-class science," says molecular virologist Mari-

ano 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



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basis of the tenure-track system, bridging the gap between postdoc and tenured position. As a result, biologists who've published a string of papers in top journals are asked to survive well into their thirties on pitiful postdoc stipends and don't even qualify for sick pay or maternity leave. "I'm not asking for a permanent position," says Enrique de la Rosa, a 34-year-old developmental neurobiologist at the Center for Biological Research (CIB) in Madrid, "I'm asking for [basic] rights." Elsewhere, he'd probably have both, but the competition for permanent biology jobs in Spain has gotten so fierce that tenure is now being given only to researchers who have a hatful of publications in top international journals. "Many professors in America wouldn't be able to get a position in Spain," claims CIB director Manuel Espinosa. "They wouldn't have enough papers."

To ease the postdocs' plight—and complete Spain's transformation into a top-rank nation for biological research—Spanish biologists almost universally offer two prescriptions. First, Spain should adopt a U.S.-style tenure-track system; and second, the government must build more labs, to open up more permanent jobs. "[T]he quantity of research in Spain is still relatively small," says CBM director Margarita Salas. On the first front, the Spanish government recently began a new program of 3-year contracts for scientists who have done at least one postdoc abroad. Senior government officials say that they want to develop a Spanish equivalent of the tenure-track system around the new contracts—there are plans, for instance, to allow contract holders to apply independently for research grants (an option that's currently open only to tenured scientists). But, much as they welcome the new contracts, most researchers argue that the number awarded this year—280 across all disciplines—was merely a drop in the ocean. As for the major expansion demanded by the biologists, the problem is that it would cost big money—and that's out of the question, at least for now.

Indeed, the new climate of austerity brought on by the global recession is already hurting every discipline. But the loudest squeals are coming from the biologists, who claim to be receiving coded signals from the Spanish government indicating that the focus of its spending is going to shift away from molecular biology, to build up areas that haven't fared so well over the past decade. Biologists characterize such a policy as punishing the successful to reward the mediocre. When money is tight, they argue, surely the best strategy is to back proven winners, like biology.

José Mato, president of Spain's national research council (CSIC), and himself an accomplished molecular biologist, flatly denies that there's any intention to squeeze biology to release money for other disciplines. But talk to Elias Fereres, a former ecologist who's now secretary of state for research in the Spanish government, and it's easy to see why Spain's biologists feel threatened. Fereres is beginning to ask some tough questions about the direction of Spanish biology, wanting more tangible social and economic returns from his government's investment. Spain's strength in *Drosophila* developmental genetics is all well and good, says Fereres, but he complains that the country's biologists don't do enough biomedical research and should be developing stronger ties with industry. "[M]any of their peers in other countries are looking more and more to biotechnology," Fereres adds. "Some of our very best scientists don't think they have to do that, and I don't feel that is fair." In their defense, Spain's biologists say that the dearth of bio-

medicine and biotechnology stems in part from the fact that there's no strong indigenous drug industry in Spain, and because molecular biology hasn't grown up under the tutelage of a dedicated medical research agency, as it has in Britain and the United States. Instead, most of the country's strongest biology labs are run by the multidisciplinary CSIC, which hasn't pressured its scientists to focus on clinical problems.

The Carlos III Institute, a government-funded biomedical agency based in the Madrid suburbs of Majadahonda and Chamartín was supposed to spearhead biomedical research in Spain, but Spanish biologists say it has produced little cutting-edge science since it

was established in the late 1980s. Some Carlos III researchers, in fact, haven't published a single paper in years. There is, however, some hope that this may change: José Borrell, formerly director of the Cajal Institute in Madrid and one of Spain's most respected neurobiologists, was drafted in to head the Carlos III in September with a mandate to reform the institute.

Borrell faces major obstacles—notably the fact that it's all but impossible to dismiss tenured staff—but if he does manage to raise the scientific standing of the Carlos III, that would go

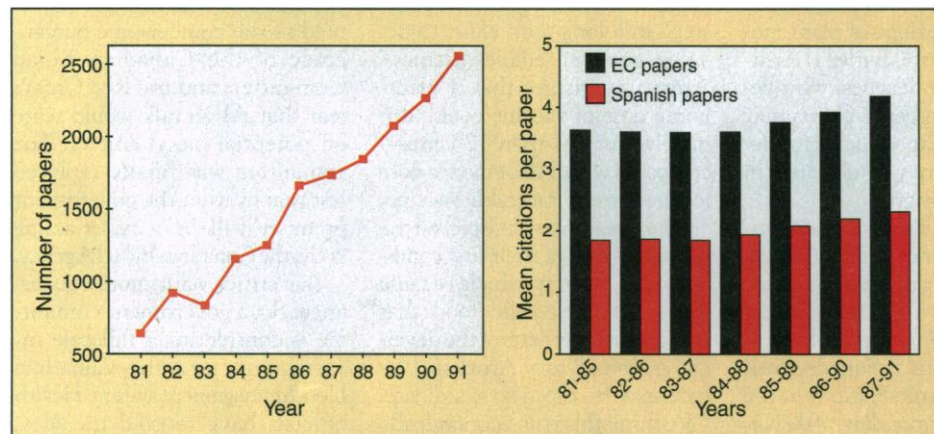
some way toward answering Fereres' complaints about the direction of Spanish biology. But Fereres makes it clear that he's also looking for a shift in emphasis from scientists within CSIC and the universities. Even when the economic gloom lifts, the signs are that the Spanish government isn't likely to build a host of new biology labs if the next generation of Spanish biologists doesn't show stronger interest in working on human disease and industrially relevant projects.

But for the current generation, the big question now is whether Spanish biology can afford to wait for an economic upturn. If that doesn't come soon, researchers fear that many of the outstanding young biologists could be lost to Spanish science—having taken permanent jobs abroad or left research altogether. If that's the case, when budgets once again increase, Spain would be struggling to regain lost ground, rather than pulling up alongside the established European powers. Says the National Center for Biotechnology's Esteban: "It will be like having a tree, not pouring on water and letting it die."

—Peter Aldhous



Too few labs. "The quantity of research in Spain is still relatively small."—Margarita Salas



Growth and impact. The number of papers published by Spanish biologists grew sharply in the 1980s (left). The number of citations per paper grew more slowly, but increased slightly in relation to the European average. Source: Institute for Scientific Information