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Changing The Way The World Does Research

Graphic: Cathleen Heard Researchers are used to stepping out of their labs to collaborate with colleagues across the hall. But with the advent of Internet technology, researchers are crisscrossing states--even oceans--to collaborate without leaving their labs.1 Nicolas Bazan, director of the Louisiana State University Neuroscience Center, New Orleans, started such an endeavor with Julio Alvarez-Builla, professor of organic chemistry at the Universidad de Alcala in Spain, six years ago. Bazan de

By Nadia Halim | October 11, 1999

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Researchers are used to stepping out of their labs to collaborate with colleagues across the hall. But with the advent of Internet technology, researchers are crisscrossing states--even oceans--to collaborate without leaving their labs. 1 Nicolas Bazan, director of the Louisiana State University Neuroscience Center, New Orleans, started such an endeavor with Julio Alvarez-Builla, professor of organic chemistry at the Universidad de Alcala in Spain, six years ago. Bazan describes the collaboration as "multidisciplinary and discovery-motivated research in neuroscience."

Bazan has been unraveling cellular and molecular events involved with neuronal response to ischemia (loss of blood flow) and to seizures.

blood flow) and to seizures.

His research focuses on retinal
degeneration, stroke, epilepsy, and most recently neurodegenerative diseases such as Alzheimer's and
head trauma. "Though these diseases seem very different, they have common denominators," says
Bazan. They follow similar mechanisms early in pathology to turn on signal transduction pathways that
lead to cell death.²

Over the years Bazan has been studying disease models and defining direct targets for drug development. When he met Builla in the early 1990s at an international conference, he found a chemist excited about creating compounds for the targets. A trans-Atlantic collaboration made sense to the two researchers despite the distance between their labs. Bazan's lab has primary neuronal cells in culture and animal models, which are used to test potential drugs synthesized in Builla's lab.

The two groups decide together which families of compounds will be synthesized to explore potential drug activity. They consider molecular modeling information provided by two groups in Madrid. Then the compounds synthesized in Spain are sent to the United States for testing. Robotic screening maximizes productivity, and the results are stored in a database accessible to both groups. Until now they have been communicating through E-mail and periodic face-to-face meetings. "We will be much more efficient with videoconferencing, since the people working in my lab will be able to interact with their counterparts in Spain. We want to maximize interaction," explains Bazan.

Another aspect of the collaboration between Bazan and Builla is the business end. They have the help of **Carlos Sunkel**, a chemist and freelance pharmaceutical adviser in Spain. He explores the business interests of the pharmaceutical field and identifies important areas of research that need further investigation. "Part of the ideas come from Sunkel, the chemistry comes from me, and the application and pharmacology come from Bazan," says Builla.

Patents resulting from this collaboration are signs of success, something neither group could accomplish on its own. The first two U.S. patents represent a family of acetaminophen analogues, which have the

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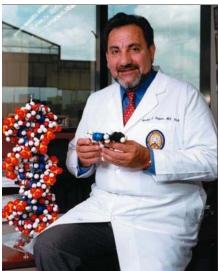
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positive effect of a nonnarcotic painkiller without liver toxicity. "This is something simple but attractive from the point of view of the pharmaceutical market," comments Builla. St. Charles Pharmaceuticals, a new biotech company in New Orleans, has licensed the patents for the two painkillers.



Nicolas Bazan

"Now we are in the process of patenting a drug that may prevent inflammation and cell death in the brain [due to injury and disease]," says Bazan. Insult to the brain starts a cascade of events that leads to the production of cyclooxygenase-2 (COX-2), an enzyme involved in cell damage. The *COX-2* gene is latent until a trigger appears, and then the tissue produces the protein. The compound being patented targets receptors inside the cell so the *COX-2* gene will not be induced to produce protein. This approach has proven successful when tested in transfected cells and in small animal models. In a way, it is a switch to prevent abnormal gene response that has toxic and damaging consequences for cells.³

Current drugs on the market inhibit COX-2 protein that has already formed and prevent it from damaging cells. "We did not want to target the *COX-2* gene promoter or transcription factors. Instead, we have identified a target upstream of the gene that will switch it off," adds Bazan. Though inhibiting the COX-2 protein has been clinically effective as an alternative to nonsteroidal anti-inflammatory drugs, preventing pathological genes from being expressed may prove valuable in the future. 4

Builla has several collaborations with large pharmaceutical companies such as Eli Lilly and Co. and Merck and Co., but he feels his collaboration with Bazan is more important. He explains, "The collaborations that we establish with academic groups often explore new fields [that] are unusual from a pharmacological point of view." Bazan adds, "I believe this type of interaction is very powerful because it creates innovation, synergy, and excitement."

Builla also points out that electronic and computer advances are opening opportunities for researchers in "noncentral countries" to do collaborative research. He defines noncentral countries as those that have not been traditionally important in scientific research. This in turn has increased funding and improved the quality of research. "I think research in countries like Portugal and Ireland is growing extremely fast due in part to collaborations with [countries such as] the United States or Japan. In Spain we have been rapidly growing in the chemical field." His group is funded 20-25 percent by the government and 75-80 percent by international industry projects. The industry funding helps pay for academic endeavors, which can be more risky.

Builla concludes, "The pharmaceutical market has been globalized for a long time, and I feel research in the pharmaceutical field should be the same. Collaborations should be established across the world with no barriers at all."

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