

Researcher analyzes last frontier: the brain

By Elizabeth Mullener

Staff writer

One day in his seventh year, Nicholas Bazan was walking through his hometown of Salta, Argentina, on his way to a piano lesson, accompanied by his Aunt Tita. They were only half a block from home, surrounded by the traditional

stucco row houses painted in gentle pastel colors and by the small trees that grew through grates in the cobblestone sidewalks.

Suddenly the music books his aunt had been carrying went flying through the air and she fell to the ground, her arms and legs flailing violently. It was a

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Dr. Nicholas G. Bazan is in the front rank of medical researchers in New Orleans, director of the Neuroscience Center at the Louisiana State University Health Sciences Center and internationally celebrated for his basic research on neurons.



STAFF PHOTO BY JENNIFER ZDON

Researcher working on new type of painkiller

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terrifying moment for a young boy.

"I didn't know what to do," Bazan says, looking bewildered even now, 52 years later. "I didn't know what was going on. It was scary. People on the street came."

What Bazan had witnessed, he learned later, was a grand mal epileptic seizure. And if he was too young to process the experience at the time, he now recognizes that the anxious curiosity it provoked in him may well have been the initiating event in his career.

Today, Bazan is in the front rank of medical researchers in New Orleans, director of the Neuroscience Center at the Louisiana State University Health Sciences Center and internationally celebrated for his basic research on neurons. With both an M.D. degree and a Ph.D., he has spent his professional life investigating the brain — its functions and dysfunctions. He continues to do research on epilepsy, but he also studies Alzheimer's disease, the effects of stroke, blinding eye diseases and the nature of pain.

In recent years, he has reinvented himself as an entrepreneur as well, starting a corporation to advance a new kind of painkiller he devised in collaboration with two chemists in Spain. It is exactly the kind of innovation the city is looking for and could well serve as the centerpiece for the long-hoped-for research and development corridor in New Orleans that could cash in on the burgeoning biotechnology economy.

But as much as he enjoys the business end of science, and the financial rewards that come with it, Bazan says he would never leave his laboratory behind. The future of his field, he says, is ripe for some thrilling advances.

"The brain," he says, "is the last frontier of medicine.

"Today you can cure so many diseases. Cancer, for example. If you make an early diagnosis,

you can cure it. But with brain diseases, no matter how early you diagnose them, we have no cure. Alzheimer's, schizophrenia, Parkinson's, stroke — these are devastating. We have some treatments for some of them, but we have no cure."

'The accidental mouse'

"Have you heard about the accidental mouse?" asks a young woman with excitement in her voice, her white lab coat flapping behind her as she sails into Bazan's office.

"I have, Mattie," Bazan says. "It is very impressive."

The mouse, they explain, is part of a research project on sleep deprivation, commissioned by the Army, that promises to bring in as much as \$11 million in grant money. The design of the experiment is to prevent the mice from sleeping for 48 hours and then immediately study the effects on the hippocampus area of the brain. The accident was that one mouse got 24 hours to recuperate before being studied. The effects of the accident were surprising — the mouse had not recovered much at all — and elucidating.

Mattie Hardy was one of a parade of young scientists in and out of Bazan's office on the eighth floor of an LSU Health Sciences building one recent morning. A corner office with commanding views of downtown New Orleans, it is crammed with plaques and awards, towering stacks of paper and a blackboard bearing a drawing of a neuron's molecular structure, as well as a collection of abstruse books, including "Neural Darwinism" and "Histology of the Nervous System."

A big and burly man, Bazan speaks with a rich Spanish accent, invoking an extensive vocabulary and an unaffected eloquence, steering his way with deliberate precision around big words or complicated thoughts. He lives with his wife, Haydee — also a neuroscientist, who works with him at LSU — in a handsome home near Audubon Park. Their five

children are grown and gone.

He goes to Mass every Sunday, drives a silver Mercedes and plays a game of tennis he describes as "enthusiastic." Like many big-name scientists, Bazan spends much of his time on the road — at meetings, conferences and seminars all over the world. At home, he spends much of his time entertaining visiting scientists.

The corner office is Bazan's command post, from which he oversees a dozen research projects that occupy 30 scientists and three floors of a sizable building. At the moment, he has about \$36 million in grant money; in the 20 years he has been at LSU, he has brought in about \$65 million.

His proclivity for research started early, when he was a young medical student in Tucuman, Argentina, and volunteered to work in the laboratory of a faculty member for a summer. It was a riveting experience, and it charted the course of his career at a time when neuroscience was just beginning to blossom. In 1970, there was no Society of Neuroscience; today it has 27,000 members. In 1970, there were only a handful of scientific journals devoted to the brain; today there is a plethora, including highly specialized ones such as "Neurochemistry" and "Hippocampus." Bazan has been at the center of some of the discipline's most exciting advances.

One of his major discoveries was the chemical changes in the brain resulting from epilepsy or stroke, as well as a way to inhibit those changes. Another breakthrough was the development of a compound that switches off the cascade of chemicals in the brain that frequently follows a head injury and kills neurons. And a third was identifying the mechanism that leads to the death of brain cells after a protracted brain disease or a sudden injury.

"Let me put it this way," he says: "In the brain cells after epilepsy or stroke or disease, there are set in motion many,

Doctor is part of advances in neuroscience

many changes. We feel the changes we are studying are the main changes. The proof is that when we block them with the drugs we've developed, we can actually protect neurons from dying.

"We need to do so much more research in this area."

Putting ideas to work

"I think in the future it will be ideas that drive economies," Bazan says. "We have service industries, we have oil, we have agriculture, and they are all very important. But the big drivers of the future will be ideas."

It was nearly a decade ago that Bazan had his own idea.

It had to do with analgesics. To be sure, plenty of analgesics are on the market, but they all have their failings. Some are narcotic; some can be toxic to the liver; some suppress fever, which serves a valuable purpose in diagnosis; and many have a

narrow margin of safety before they bring on harmful side effects.

After decades of studying the brain and its diseases, Bazan had developed some notions about viable targets for drugs within the brain. He began working in his laboratory on a purer analgesic. It was in 1993 that he struck up a cyber-collaboration with the two Spanish chemists, at the Universidad de Alcalá. Together, they came up

with a compound for a painkiller that avoids all the usual pitfalls. They call it SCP-1.

The leap from pure research to a medical application was exhilarating for Bazan.

"What an MD scientist like me does every day — ultimately, one would like to see this applied," he says. "One would like to see the transfer of knowledge from the research

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bench in the laboratory to the bedside of the patient. Every scientist would like to do that."

Since the invention of SCP-1, which could be a rival to Tylenol, Bazan has acquired three patents for the compound and has started up a corporation, St. Charles Pharmaceuticals, to test the drug, refine it and eventually produce it. Along the way, he snagged \$4 million in local venture capital to keep the enterprise going.

The new direction in Bazan's life required some professional retooling.

"I was telling my children that doing all of that was like getting a mini-MBA degree," he says.

Meanwhile, St. Charles Pharmaceuticals — with eight full-time employees, 15 consultants and offices one floor up from Bazan's — has been charging ahead with its mission. A few weeks ago, the Food and Drug Administration approved SCP-1 for clinical trials in human beings. The trials, already under way in Austin, Texas, have been encouraging, showing no toxicity and no side effects. The next step is to test the drug for effectiveness. It could hit the market within three years. Bazan is delighted with the progress.

"We're on a roll," he says.

Culture of innovation

The city of New Orleans would like to think so. A biotechnology corridor downtown, with nearly 20,000 medical workers in its midst, has long been a dream of those planning for the city's future. The invention and production of a mass-market drug would be an ideal kickoff for such a venture. It has drawn the attention, and the enthusiasm, of Gov. Foster, who has proposed a \$150 million plan to stimulate scientific research in Louisiana, a move he predicts could spin off scores of profitable businesses and provide high-paying jobs for tens of thousands of workers.

Bazan agrees the potential is there.

"I would like to see many of these companies here, startup pharmaceutical biotech compa-

nies," Bazan says. "We could develop 100 companies. That is not impossible.

"I am completely convinced there are many assets in the universities and colleges here, and to some extent in the business community. If they can be brought together, they can help create a totally new force for our economy. The opportunity here is to create in the New Orleans region a culture of innovation, a culture where many people are involved: lawyers that deal with intellectual property, accountants, finance people.

"It works both ways. The universities provide the creative force and the community captures that and nurtures it." Besides St. Charles Pharmaceuticals, there are other possibilities for startup companies inherent in Bazan's research. One is a patented molecule he has developed with a potential to treat epilepsy. Another patent could lead to a drug to limit the damage to the brain after a stroke. A third is for a family of chemicals that could slow down the progress of Alzheimer's disease.

And many other scientists in town have ideas ripe for development. Bazan foresees New Orleans taking up a niche in the biotechnology world, probably in the areas of neuroscience, gene therapy, cancer or ophthalmology. He even foresees the possibility that some of the giant pharmaceutical companies might create partnerships with local universities and possibly set up branches nearby.

"New Orleans could become as well-known in those fields as Houston is in cancer and cardiovascular," he says.

"I don't want to appear to be oversimplifying this," he adds. "This is not easy. Our assets are small compared to other cities. In San Francisco, if somebody says, 'I have an idea' — boom, they will get a building, they will get venture capital. It's all available. It's not so readily available here. But I am very optimistic that it can be done.

"I don't want to say anything bad about the Saints or the Hornets or the casinos. I love

the Saints. But I think we put too much emphasis."

Living in mortal danger

When Bazan arrived in New Orleans in July 1981, it was by the skin of his teeth.

Argentina at the time was going through a turbulent period politically, rocking from extreme left to extreme right in one revolution after another.

"Out of this clash there were 30,000 missing people," Bazan says. "The *desaparecidos*. The disappeared. They would be tortured, then thrown into the sea."

Bazan, although never politically active, was nearly one of them.

He joined the faculty of the Universidad del Sur in Buenos Aires province in 1970, after holding research posts at Columbia University, Harvard University and the University of Toronto. For the next 11 years, he worked under a series of university presidents, all politically appointed. The last one didn't take kindly to Bazan's refusal to go along with the school's harsh new strictures, nor did he take kindly to the Jews on Bazan's faculty nor to his father's past as a middle-level politician in Juan Peron's government. Before long, Bazan's name appeared on a blacklist. Accused of being a terrorist, he was fired from his job and banned from teaching and research.

"This was at the end of 1980," Bazan says. "By then there was a worldwide outcry against the killing of all those people. If this had happened one year earlier, for sure I would not be able to tell you this story."

Once fired, Bazan became a media celebrity of sorts. Coverage of his research already had appeared in the Argentine newspapers. But at this point, crusading journalists all over the country used his case as an example of oppression by the military regime. They wrote hundreds of articles and editorials about him.

"I even wrote articles myself with my signature in the newspapers about science and freedom," he says. "I wrote about

why it was so important for Argentina, a poor country needing development, to have scientists and educators."

The more Bazan became a cause célèbre, the more the government bore down on him. For three months, he lived in mortal danger.

"A lot of nasty things began happening," he says. "There were many phone calls, many threats. They tried to intercept my car. I escaped. They tried to kidnap me. I went into hiding. But the news people kept calling me and I would keep talking. Then I got a phone call saying if I speak to one more reporter, they will hurt me and my family."

In the meantime, because of his international renown as a scientist, Bazan's case came to the attention of three U.S. senators. It also came to the attention of Herbert Kaufman, chairman of LSU's ophthalmology department.

Shortly thereafter, Bazan got a phone call from the American embassy in Buenos Aires. Suspecting that his phone was tapped, they invited him — with a wink in their voices that he understood — to come talk to the ambassador about his research. He went.

"The ambassador told me he knew I was in trouble, and they were prepared to take me out of the country," Bazan says. "We closed our home and left. The cultural attaché took us to the airport, with a photographer to document we were there. We arrived in Miami without a visa."

That night, Bazan flew into New Orleans with his wife, five children, seven suitcases and two boxes of research results. No more. The next day, he went to work for Kaufman and LSU.

He has been back to Argentina, now much more settled politically, many times since. He has been given honorary degrees and awards there; he has even been offered his job back.

"Of course, I didn't take it,"

he says, shaking his head. "America is my country. This is where my heart is — and my mind. My children are here, my grandchildren are here, and all my colleagues. I love New Orleans. I love Louisiana. I want to contribute here, to work here, to be constructive."

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