

Back on Track: Saving Lives

After fleeing Cuba, this medical student tested a new treatment for heart attack.



CUBAN-BORN FELIX GONZALEZ decided early that he wanted to be a doctor. At age 16, he entered medical school. Three weeks into his studies, however, soldiers burst into his classroom, lined up all the young men, and took them to be enlisted in the Army. “I had been training how to save lives,” says Gonzalez, “and now they were training me to take lives.”

Fast-forward 12 years. Gonzalez is close to earning his U.S. medical degree. During two years as an HHMI-NIH Research Scholar, the tenacity that helped him recover his dream led to findings that may yield a new therapy for heart attack patients.

With lead investigators Mark T. Gladwin and Andrew E. Arai at the National Heart, Lung, and Blood Institute, NIH, Gonzalez showed that a ubiquitous chemical, nitrite, can prevent cellular damage in dogs after a heart attack, and the treatment has moved into human studies.

During a heart attack, when blood supply to the heart muscle is blocked, the lack of oxygen kills some heart muscle cells through necrosis, a process in which the cells’ internal parts break apart. Treatments such as drugs, stents, and balloons aim to open blocked arteries to improve blood flow after a heart attack. The return of oxygenated blood (reperfusion), however, can cause a

Nitrite may have a place in rescuing heart muscle cells after a heart attack, according to research by medical student Felix Gonzalez and his NIH mentors.

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second round of damage. Remaining cells become stressed and begin the process of apoptosis (cell suicide) instead. Apoptosis may be triggered by reactive oxygen species—unstable molecules containing oxygen—which deliver a final blow.

This study confirmed that nitrite improved the percent of heart muscle that was salvaged by restoring blood supply to the heart. Nitrite also dilates veins and arteries, which helps restore blood flow to cells at the center of the affected area. Additionally, nitrite seems to protect the cells from reactive oxygen species, reducing apoptosis.

The researchers used magnetic resonance imaging to observe dog hearts before, during, and after a simulated heart attack in which blood flow in the coronary arteries was blocked and then restored. About 70 percent of heart cells deprived of blood died in the untreated control animals. In dogs treated with nitrite for an hour before reperfusion, however, fewer than a quarter of the heart cells died. The results of the study were published June 10, 2008, in the journal *Circulation*.

Importantly, a second group that received nitrite for only five minutes before reperfusion recovered almost as well, with about 36 percent cell damage. “It means that you could be treated with nitrite while you’re being prepared to be catheterized [to remove artery blockages] with no time lost,” says Gonzalez, the paper’s first author.

With this paper and an early, or phase 1, safety study in human volunteers complete, Gladwin, now at the University of Pittsburgh Medical Center, is pursuing funding to

carry out a phase 2 clinical trial in heart attack patients.

Testing each subject required 22 hours of continuous work, and Gonzalez sometimes did two tests a week. “It took very physically grueling work to get the data,” says Arai, Gonzalez’s mentor and a cardiologist skilled in imaging techniques. “Felix did an outstanding job.”

Gonzalez had years of practice being resolute and working hard. Soon after he

Jersey’s Kean University, which offers courses in Spanish and English, he earned a B.S. and was accepted at several medical schools and two M.D./Ph.D. programs. They offered scholarships, but he was suspicious, he says, since in Cuba, free education came with strings attached. He decided to enter the Robert Wood Johnson Medical School in New Jersey, and to apply separately to research programs. He hopes

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was conscripted, he decided to leave Cuba. It took a year of planning, some deception, and luck to gain permission to go to the United States. Still, on departure day, he felt torn. His parents had separated when he was 3 years old, and he felt guilty leaving his mother behind.

“It was the uncertainty that made it difficult. I wasn’t sure when I would see her again,” he says, recalling that day at the airport. “She told me, ‘When you start something, you have to finish it.’”

When he reached the United States, Gonzalez received some support from a Cuban-American organization and his estranged father, a factory worker who had moved to New Jersey years earlier. After a few months, Gonzalez began to support himself as a dishwasher while he studied English. For a time he lived out of a small car.

Gonzalez still dreamed of having a medical career. After studying at New

to specialize in interventional radiology and to continue his involvement in research.

Two years ago, after becoming a U.S. citizen, he helped his mother move to the United States. It had been more than a decade since he had last seen her.

“I think I have had success because of my perseverance,” Gonzalez says. “If I really want something, I don’t ask permission—I just do it.” He says he hopes those still living in Cuba will also someday have better career opportunities. “I would like to see more freedom and economic investment in Cuba, so people can make their own life choices.” ■ - KATHLEEN O’NEIL