

Magnet may be cure for our ills

900 megahertz nuclear magnetic resonance spectrometer for research

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Dr. Michael Weiss used to dream about being able to see how insulin binds to human cells and sometimes gives rise to diabetes.

But since the largest research magnet of its kind was installed in December at the Cleveland Center for Structural Biology, Weiss and his fellow researchers no longer have to dream.

Using the huge magnet, called a spectrometer, researchers can see large molecules, such as the misfolded proteins that can destroy blood vessels and organs in diabetics.

This and other equipment at the center could help researchers develop drugs and technologies that cure disease -- and eventually help manufacturers create jobs and wealth for the region.

The installation of the 900 megahertz nuclear magnetic resonance spectrometer represents the end of a more than decade-long effort to put Cleveland in the "top league" of biological imaging research communities, said Paul Carey, the center's director.

"We have arrived," said Carey, a biochemistry professor at the Case Western Reserve University School of Medicine who was hired in 1994 to help lead the effort.

Marjorie Tingle agrees. She oversees the National Institutes of Health High-End Instrumentation grant program that contributed \$2 million to the purchase of the 900. "With only about a dozen of this type of spectrometer available to researchers across the country, this places the Cleveland Center for Structural Biology at the cutting edge of nuclear magnetic resonance technology," Tingle said in an e-mail interview. The spectrometer also could help the center attract faculty and more research grants, she said.

The center began in 1994. "There were senior scientists at the Cleveland Clinic and Case [who] felt the scientific community was behind the curve, in terms of being able to undertake molecular structure imaging," Carey said.

So the researchers -- whose clinical colleagues and institutions compete fiercely for patients -- put their heads together and hatched the idea for a structural biology center that could be used by all researchers.

"This was revolutionary," Carey said. "It involved cooperation between two institutions that had been competitors."

Cleveland State University, MetroHealth Medical Center and University Hospitals of Cleveland (Case's primary academic affiliate) have since joined the center.

Cooperation enabled the researchers to land at least \$15 million in grants and state capital improvement money since then. The money helped build the structural biology

building at Ansel Road and Mt. Sinai Drive, buy powerful imaging equipment and woo heavy-hitting scientists, such as Weiss.

The center started with a \$2.25 million grant from the Cleveland Foundation in 1995.

The researchers' grant proposal laid out a thoughtful way to capitalize on the nuclear magnetic resonance imaging strengths of the Clinic and the X-ray crystallography expertise of Case and University Hospitals, said Bob Eckardt, senior vice president of the foundation's programs and evaluation. "The foundation doesn't often make grants in the area of medical research," Eckardt said. But when it does, the money must be used to "increase this community's ability to compete in the region."

In addition to buying expensive, top-of-the-line imaging equipment, the plan called for recruiting scientists to Cleveland through joint search committees, which required unprecedented cooperation among former competitors.

At first, there were a lot of questions, Eckardt said. "Could they really do joint recruitment sessions? Could they be an integrated team? Every hurdle they have cleared successfully."

The center used the foundation's grant to buy its first instrument, a 600 MHz nuclear magnetic resonance spectrometer, Carey said. Much of the center's initial equipment was housed in a former furniture store on Carnegie Avenue. Some of it was located at the center's institutions.

The collegial spirit among the researchers attracted more grants. "Because of the perception that things were changing, that we were getting into an era of collaboration instead of competition, local and state funding kicked in," Carey said.

More equipment was purchased and scientists were hired.

"We needed more in terms of high-end nuclear magnetic resonance equipment," said Edward Plow, chairman of molecular cardiology at the Clinic. So the researchers again petitioned the Cleveland Foundation.

In 2001, the foundation made a grant to expand the center and buy the 900 MHz spectrometer, this time for \$3 million.

The center now includes 900, 800, 600 and 500 MHz nuclear magnetic resonance spectrometers, as well as a 300 MHz solid-state instrument. Many of the instruments are at the center building. Additional spectrometers are at the Clinic and Case.

The center also includes X-ray crystallography equipment, which is at the Clinic's Lerner Research Institute, Plow said.

In addition, the center belongs to a 10-institute consortium that gives it access to the most powerful spectroscopy equipment, housed at the Lawrence Livermore National Laboratory in Livermore, Calif., Plow said. "With these new instruments, we have really been placed on the map," he said. "We are as well-equipped as any other city, in terms of having high-end instrumentation available to our investigators."

The researchers expect the center's equipment to draw academic and commercial investigators from Akron, Columbus and Cincinnati, as well as from outside the state.

"The center's ability to compete for other grants, the quality of the people it is getting, and the quality of research that is coming along tells us that we are in the top league" of research communities, Eckardt said.

At the same time, Jeffrey Duerk, director of the Center for Imaging Research at the Case Research Institute and vice chairman for basic science research in Case's radiology department, won several grants for studying humans and small animals.

Though not part of the Cleveland Center for Structural Biology, the Case and University Hospitals equipment strengthens Cleveland's boast as a top biological research community.

This imaging equipment helps translate what scientists learn on the molecular level to the human patient level, Duerk said. "There are few places that have as good an infrastructure as we do in many modalities," he said.

Duerk and his colleagues also wrote the proposal that snagged the \$2 million NIH grant in 2003. That money helped buy the latest arrival to the structural biology center – a Bruker BioSpin spectrometer that only a dozen or so U.S. centers have.

Since mid-December, local researchers have been overseeing the installation of the machine by a German engineer.

Pumps have been slowly drawing the air from the vessels inside the spectrometer, creating a vacuum. Miles of magnetic wire coiled inside will create two-dimensional "pictures" of large molecules on computer screens behind tempered Plexiglas windows.

Three more spectrometers share the center's sealed room, which would protect researchers from hydrogen and helium gases if there was an equipment failure.

Frank Sönnichsen, associate professor of physiology and biophysics at Case, went to Germany to see the spectrometer in 2001. The center purchased the machine in 2002. "Now, it's finally here," said Sönnichsen, who was one of the scientists recruited to Cleveland with the structural biology grants. "It's been gratifying seeing this facility come together."

Weiss, who is chairman of Case medical school's biochemistry department and co-chairman of its diabetes task force, is eager to see the magnet's first images of insulin. "These magnets give pictures of molecules like MRIs give pictures of the body," Weiss said. Because the spectrometer's magnet is 20 times more intense than magnetic resonance imaging equipment used on patients, researchers can "look at the insides of molecules," he said.

The center and its equipment and expertise could do a lot for the scientific community. What could it do for Greater Cleveland? "It does two things," said the Cleveland Foundation's Eckardt. "It shows that when we figure out a vision and work on it for a period of time, we can move into the [nation's] top tier."

It also means the region has strengths that can foster research "that has the potential to support economic development long term," Eckardt said. "So many communities are betting on biotech. You can't succeed if you're a 'C' player. You have to be an 'A' player."