Technological Revolution

STORY BY JOHN BEAHLER

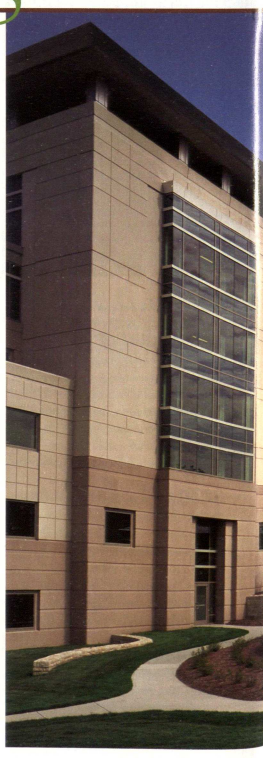
COOPERATIVE RESEARCH ACROSS THE STATE'S INTERSTATE 70 BIOTECH CORRIDOR PROMISES ADVANCES IN FOOD, HEALTH AND THE ENVIRONMENT. IT'S ALSO GOOD FOR THE ECONOMY.

JIM STOWERS HAS ALWAYS SET HIGH goals for himself. As a student at Mizzou in the late 1940s, Stowers earned a bachelor's degree in chemistry, then turned right around and plugged away until he finished what was then the two-year medical degree program at MU.

As a businessman, Stowers pioneered the use of computers to manage mutual funds. In the process, the Kansas City, Mo., native built an investment of a few thousand dollars into the financial powerhouse that today is called American Century Investments.

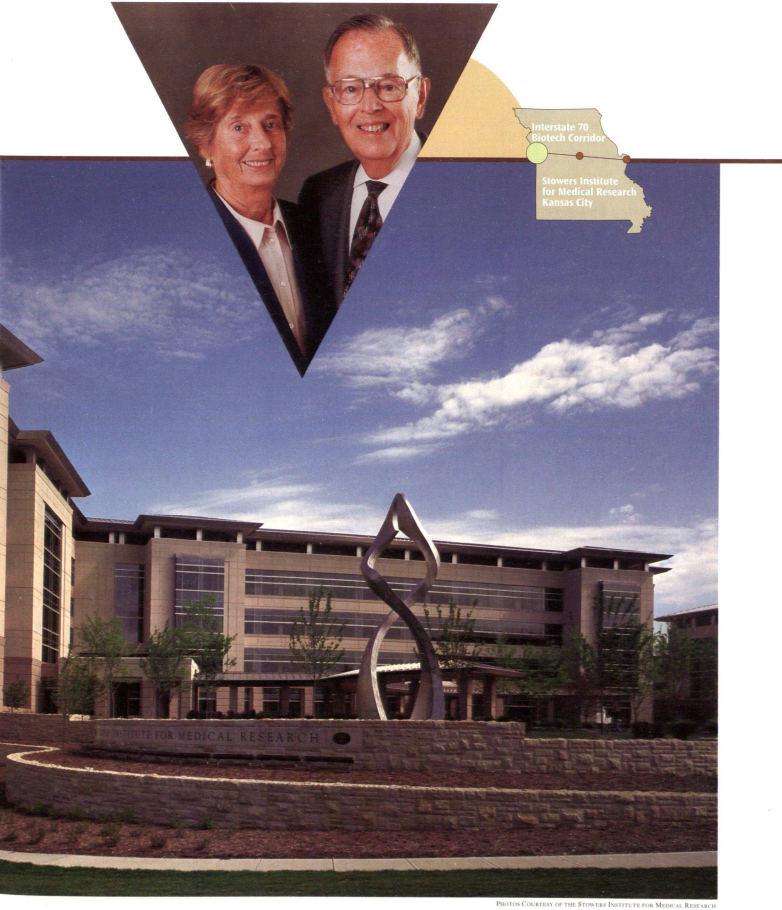
In his second career as a philanthropist, Stowers and his wife, Virginia, who are both cancer survivors, have dedicated their personal fortune to an even more formidable objective. The couple established the Stowers Institute for Medical Research with an endowment that currently stands at $1.6 billion. Their goal is to gather some of the world's most outstanding scientists at the Kansas City research center and give them the tools to tackle the toughest basic questions in medical research.

Stowers foresees a "biomed valley" that would turn Missouri into a major player in life sciences research and innovation, much like California's Silicon Valley is known for computer technology. The Stowers Institute is playing a significant role in anchoring the western end of the biotech corridor, which stretches through Columbia and the heart of the Mizzou campus. Its eastern limits would be in the St. Louis area, where another



MU alumnus and mutual fund pioneer Jim Stowers and his wife, Virginia, inset photo, have dedicated their personal fortune to a medical research center that offers hope to people with illnesses considered incurable today.

The Stowers Institute for Medical Research is part of a scientific renaissance in the heart of Kansas City, Mo. The 10-acre campus near the Country Club Plaza is at the western terminus of Missouri's Interstate 70 Biotech Corridor, which includes Mizzou. Scientists at the Stowers Institute are exploring some of the basic questions about how genes function.



Photos Courtesy of the Stowers Institute for Medical Research
Hope for Life Sculpture by Larry Young

world-class life sciences research facility — the Donald Danforth Plant Science Center — is attracting top scientists to its ambitious research agenda.

"If we do this right, the benefit to society will be fantastic," Stowers says. He points to potential cures for the most intractable diseases, from cancer and diabetes to arthritis, and heart and kidney disease. The institute's scientists are conducting basic biomedical research on the ways that genes control disease processes.

"The economic benefits of this research can be almost as fantastic," Stowers says. Successful research along this burgeoning biotech corridor could mean an economic boost in business spin-offs from the research and in more high-paying jobs for Missourians.

Stowers' ideas are shared by some of Missouri's top political leaders. Gov. Bob Holden, in a speech to MU supporters earlier this year, called investments in life sciences research a key to Missouri's economic future.

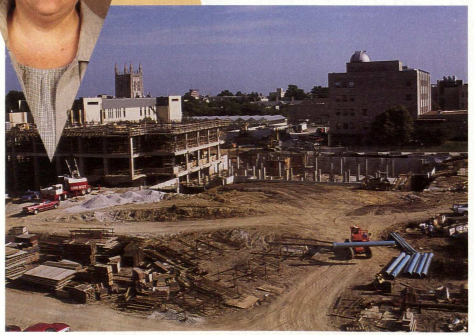
"I don't want Missouri just to be one of 50 states in this global economy; I want us to be a leader," he said. "You don't do that without a commitment to education, and I don't believe you do that in Missouri without a commitment to life sciences.

"When people talk about the economy of the 21st century and what the keys are going to be, they talk about food and they talk about medicine, and both of them are based in the life sciences."

Last fall, Holden helped make a reality of Mizzou's longtime dream for a life sciences research initiative. The governor approved the first state appropriation to build a new Life Sciences Center on the MU campus. The state is matching nearly $30 million in federal funding for the new center. U.S. Sen. Kit Bond championed the federal investment in the research center, now under construction at the intersection of Rollins Street and College Avenue on the southeast side of campus. The building, to be completed by fall 2004, will become Mizzou's showplace for interdisciplinary research in life sciences.

Collaboration could be a key to solving the scientific riddle that MU biologist Cathy Krull, inset, is unraveling: How do molecular signals guide cell migration during embryo development? Finding the answer could be the first step in creating new treatments for diseases.

Mizzou's new Life Sciences Center, below, scheduled for completion in 2004, will help forge new partnership possibilities between MU researchers and scientists at research centers around Missouri.



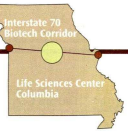
Construction Photo by Rob Hill; Portrait by Steve Morse

A conference on campus this past March underscored MU's central importance to this statewide initiative. Life science leaders from around Missouri gathered at Mizzou to address the potential for an Interstate 70 Biotech Corridor that stretches across the Show-Me State.

"Biotechnology is the next technological revolution," Sen. Bond told those attending the conference. "Here in Missouri, we have the leaders in the field. The biotech corridor will be the place people look to for advances in the 21st century.

"We see scientists leaving European countries and coming to Missouri. The hostile environment there is driving them out. Well, their loss is our gain. Missouri can be a real leader in providing this technology." To acknowledge Bond's long-standing support for life sciences, the new research center will be named in his honor after he retires from political office.

Mizzou's long track record of promising work in medical research prompted U.S. Sen. Jean Carnahan to pledge her support for a $30 million infusion of federal funding to finance a new health sciences research center at MU. Although the proposed health sciences facility is still years down the road, the center, estimated to cost $136 million, would be the first new research space built for the



School of Medicine in four decades. It would help boost research funding from the National Institutes of Health, and could be key to MU's push to be designated as a Comprehensive Cancer Center by the National Cancer Institute.

During a campus visit in May, Carnahan praised MU's efforts to treat and solve chronic health problems, and acknowledged that her announcement was only a first step in a long and complicated federal appropriations process. She also noted that Missouri ranks above the national average in the incidence of some types of cancer, diabetes and heart disease.

"The speed and extent of innovation can outstrip the imagination. We are sometimes unable to bridge the gap between discovery and delivery," Carnahan said. "This new center will help link cutting-edge research and hospital and clinic applications. The pace of research makes it possible that we will see cures in our lifetime."

THE NEW LIFE SCIENCES CENTER might be the most visible aspect of Mizzou's campuswide initiative, but scientists here have been making groundbreaking discoveries in the plant sciences for more than a century. In recent years, MU researchers have become national leaders in the exciting scientific developments that will fuel future discoveries.

Geneticists are unraveling the genomic maps of important food and fiber crops. What they learn could help feed a hungry world. With the unique resources of the University of Missouri Research Reactor Center, scientists are making breakthroughs in radiopharmaceutical drugs to diagnose and treat cancer. Medical researchers are joining with MU engineering faculty to harness high-speed computers and put them to work to find disease cures.

The list of life sciences research at Mizzou goes on and on. Now, with the burgeoning connections between campus and other research enterprises, the potential has never been greater.

For MU biologist Cathy Krull, the ability to collaborate with top scientists at the Stowers Institute opens up exciting research possibilities. Krull studies how molecular signals control cell migration during embryonic development.

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"Just as highway traffic is controlled by signs and signals, cell migration also is guided by molecular signals that tell cells where to go and how to grow," says Krull, assistant professor of biological sciences.

"If we can learn how cells are guided and how they respond, we might be able to use that information to find new treatments for a number of diseases." One day, scientists might be able to create cancer treatments by using a molecular "stop sign" that inhibits tumor growth. Or perhaps researchers could learn how to reconnect damaged spinal cords.

Krull has forged a collaboration with Robb Krumlauf, the Stowers Institute scientific director and, like Krull, a developmental biologist. The two scientists have published a joint paper and are cooperating on several research projects.

"These kind of collaborations are hard because you can't force them by picking names out of a hat," she says. "It doesn't work that way. These type of collaborative relationships happen naturally when scientists have a lot of exposure to each other."

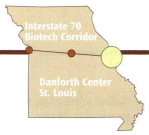
Krumlauf says that he welcomes the broad expertise in basic sciences that MU can bring to the table. "In all areas of research it is impossible for any one person or team to have all the knowledge, technology and expertise needed to solve complex research problems," he says.

"Researchers routinely need to utilize whatever approach or experimental system best addresses the problem under investigation. For example, scientists are no longer focusing all their attention on a single gene or protein in isolation. They want to know how these molecules normally function in integrated networks and how they go wrong in disease."

The result is that researchers are changing the way they approach their science, Krumlauf says. "Cutting-edge technology is expensive, and all institutions find it difficult to strike a balance between meeting mainstream needs and setting up special technologies that might only support a few researchers.

"Collaboration and the sharing of expertise between scientists and between institutions is an essential and efficient way of driving research. Besides, it's fun to interact with other scientists like Cathy Krull and share ideas on complex biological questions."

In addition to tapping into the intellectual capital that such collaborations offer, MU nutrition scientist David Eide will be able to call on the newest scientific infrastructure at the Danforth Plant Science Center in St. Louis. Eide studies how



yeast cells absorb the essential nutrients of zinc and iron. His lab has identified genes in baker's yeast that produce proteins to regulate the process. When zinc or iron are relatively scarce in the environment, certain proteins in the yeast cell enhance the uptake process. If there's too much of these metals available, other proteins reduce the uptake so they don't reach toxic levels.

"These are critical questions for plant biologists, because iron is one of the major plant nutrition problems in the world," says Eide, an associate professor of nutritional sciences in the College of Human Environmental Sciences. "As it turns out, the mechanisms that plants use are very similar to mechanisms that humans use, so we all learn from each other."

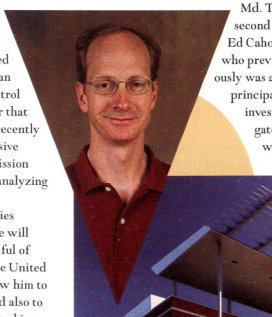
Soon, he'll have the opportunity to learn even more. For several years, Eide has been working with plant scientist Dan Schachtman, who recently joined the Danforth Center. Schachtman is working on the genes that control zinc uptake in wheat. To further that research, the Danforth Center recently acquired a vital and very expensive piece of equipment — a transmission electron microscope capable of analyzing metal ions.

Thanks to the collaborative ties between the two scientists, Eide will have access to one of just a handful of such microscopes available in the United States. The microscope will allow him to measure metal levels in a cell and also to pinpoint where they're distributed in a cell. "This is work that we really have needed to do," he says. "I'm looking for great things from our collaborations with the Danforth Center."

More cooperative research ventures are taking root between MU and partners around the state. The federal Agricultural Research Service's (ARS) plant genetics unit headquartered at Mizzou has hired two outstanding scientists who will be based at the Danforth Center. That will put MU on an equal footing with "soybean research powerhouses" such as Illinois, Iowa and North Carolina universities, says Larry Darrah, a plant geneticist who heads the ARS Plant Genetics Research Unit located at Mizzou. The ARS is a unit of the U.S. Department of Agriculture.

One of those two new soybean scientists is Eliot Herman, a former top researcher at the ARS unit in Beltsville, Md. The second is Ed Cahoon, who previously was a principal investigator with DuPont Crop Genetics. Cahoon plans to work with seed quality improvements in such areas as producing industrial oils from soybeans. Especially promising will be work on developing a better drying soy oil, so that soy ink sets faster with less smearing.

"There is every likelihood that with the Danforth Center, we can get more visiting scientists from around the world," Darrah says. "There will be great opportunities for collaboration."



Cooperative agreements between Mizzou and the Danforth Plant Science Center in St. Louis, right, will give nutrition scientist David Eide, inset, access to vital research equipment there. Eide studies how genes regulate the uptake of essential nutrients like iron and zinc in yeast cells. His findings could be significant for plant nutrition and for human health.

Building Photo Courtesy of the Danforth Plant Science Center; Portrait by Steve Morse

ALTHOUGH LIFE SCIENCES SHOW incredible promise for medical and agricultural advances, not everyone agrees they are the wave of the future. Some critics raise concerns that genes added to bioengineered plants could escape and crossbreed with other plants in the wild. Bt corn, for instance, contains a gene from a bacteria that produces a toxin that targets the European corn borer, a major agricultural pest. One early laboratory study suggested that pollen from genetically altered corn containing the same toxin could contaminate nearby

plants that monarch butterflies feed on as caterpillars. Later field studies discounted that possibility.

Still other critics see a bumper crop of economic evils sprouting from the new technology. Relying on a few strains of corn or cotton or soybeans reduces the global gene pool, they say, and lets a handful of corporate Goliaths call the shots and set the prices. That kind of consolidation, they argue, could bring small producers and family farmers to their knees.

"All these arguments are being made. I'm not really sure that biotechnology is posing or even necessarily fueling any of this, but it's certainly part of the equation," says agricultural economist Nick Kalaitzandonakes. "Consolidation of the family farm would have happened even in the absence of biotechnology."

Kalaitzandonakes is director of the Economics and Management Agrobiotechnology Center at MU, a policy think tank and research center that studies the impact of biotechnology on agriculture.

Some observers argue that biotechnology is triggering a wholesale consolidation in the agribusiness sector, but Kalaitzandonakes poses a counterargument: Consolidation isn't just targeting agriculture, he says. It's a trend that's sweeping through our economy for a number of reasons. Take food retailing, for example. America's mom-and-pop grocery stores are giving way to superstores and multibillion-dollar supermarket chains that leverage advances in information technology and management techniques to create cost savings, part of which are passed on to consumers.

"They basically force other retailers to consolidate," he says. "Large retailers tend to want to deal with large suppliers because it simplifies the way they connect with one another. So that has forced manufacturers and distributors to consolidate. It's a chain reaction."

That chain reaction goes all the way back to the agricultural sector that competes to sell its products to the giant food processors and supermarket chains.

The biotechnology industry is no stranger to consolidation itself. In the five years since biotech took off, there has been a rash of buyouts with big players snapping up smaller companies. Kalaitzandonakes argues that this consolidation comes not from the new technology these companies invented, but is part of the standard life cycle of innovation and adheres to basic economic principles that were operating long before farmers harvested their first bioengineered crop. It's much the same phenomenon that's taking place in e-commerce and telecommunications, he says, and for the same reasons.

AFTER YOU'VE DEVELOPED THE TECHNOLOGY, WHETHER YOU PUT IT IN ONE BAG OF SEED OR 80,000 BAGS, THE COST IS NO DIFFERENT.

"All of these businesses have the same basic cost structure, which is that you have to spend a lot of the money up front and make the investments to develop the technology or build the infrastructure," he says.

"But after you've developed the technology, whether you put it in one bag of seed or 80,000 bags, the cost is no different. It's the same thing with telecommunications. After you put a satellite up there, you can use it for five customers or 5 million."

And, if biotech firms have poorly protected or overlapping patents — which many did — a price war quickly develops as they try to sell that technology to customers. "Competitive bidding drives down the cost of that technology to zero or close to it," Kalaitzandonakes says.

That's what sparked a second wave of consolidation in the industry. Giant corporations such as Monsanto and DuPont rushed to buy biotech and seed companies so they could protect and market their technologies.

"Biotechnology probably has had very little effect on consolidation in the agricultural sector," Kalaitzandonakes says, "because it's what economists call 'scale neutral.' That means that if you have a 200-acre farm and I have a 5,000-acre farm, I don't have an inherent advantage over you by planting bioengineered crops.

"Biotech has probably increased yields by a little bit, but not by much. Because the new crops that ultimately have come to the market — Bt corn, Bt cotton or Roundup Ready soybeans — are mostly input reducing, not yield increasing. The majority of the impact has been on reducing costs."

That means farmers have to apply far less of an expensive pesticide to kill crop-damaging insects. Or, by using Roundup Ready beans, it's more feasible to switch to no-till cultivation and save money on tractor fuel and planting costs at the same time farmers reduce soil erosion and pollution. (See "Boon to Beans," Page 23.)

"There are substantial profitability gains, both in the United States and elsewhere," he says. "Otherwise you would not see the kinds of adoption rates that you are seeing. Argentina went from 0 percent to 90 percent of their soybeans being Roundup Ready in four years; our beans in the United States are 70 percent Roundup Ready in five years. You can't do that with unprofitable technologies."

But perhaps the greatest potential impact of bioengineered crops is for small farmers in developing countries, Kalaitzandonakes says.

One study in China found that in some

locations chemical insecticide use on cotton went from 30 applications in a season down to two. Another study in Mexico showed that it was economically viable to plant Bt cotton in areas where the cotton crop had been abandoned because of the need for expensive chemical pesticides.

Whether they're grown on the plains of China or the Great Plains of the United States, an added benefit of bioengineered crops is environmental, Kalaitzandonakes says. They rely less on chemical pesticides, and the herbicides they do need are less toxic to humans and animals.

He points out that genetically altered food plants are some of the first agricultural products to come from the explosion of knowledge in the life sciences. "What you are looking at are first-generation products that are typically clunky and can afford a lot of improvement. That's true for any major innovation," he says.

"So you have a set of products that are performing — not everywhere and not for everybody, but for a large number of agriculture producers — very productively and very profitably. Perhaps more significantly, these products are also yielding significant environmental benefits, and that could be of interest to all."

As MU builds on past successes to expand its life sciences initiative, the campus is committed to nurturing the research that will translate into critical benefits for the state and for people around the world. The biomed valley that Stowers envisions is becoming a reality in Missouri.

"Our first goal in nurturing a life sciences corridor is to become a powerhouse in the discovery of new knowledge. That provides the foundation for all to follow," says MU Chancellor Richard Wallace. "We must encourage entrepreneurship, and at the same time we must preserve the freedom of inquiry. One of our missions is to provide the types of education that we need to develop our state's potential in the life sciences." ❋

Photo by Rob Hill
Soybean Photo by James Fashing, BJ '93, Courtesy MFA Incorporated

Boon to Beans

FROM IMPROVING FAT CONTENT TO FINE-TUNING SCHEDULES FOR SPRAYING HERBICIDES, MU SCIENTISTS HAVE SPENT YEARS DEVELOPING SOYBEANS ESPECIALLY FOR MISSOURI FARMERS.

MOST MISSOURI SOYBEAN FARMERS will tell you that if they aren't growing Roundup Ready plants, they're producing hasbeans. Scientists have improved yields of Missouri's top cash crop and made it easier and cheaper to grow by implanting hardy soybean varieties with the Roundup Ready gene. The gene immunizes beans against herbicides that kill other plants just inches away — weeds like common water hemp that reduce bean yields by competing for water, sun and soil nutrients. These genetically modified plants became available in 1995, and already 80 percent of Missouri's farm acres in soybeans grow Roundup Ready varieties.

Scott Morse, BS Ag '80, of Harrisonville, Mo., says he wouldn't farm any other way. He plants 55 acres of soybeans on his family farm after harvesting wheat in the same field. With conventional beans, he'd have to till the soil two or three times to prepare it for planting. "I don't have that time," says Morse, who also is an investment broker at Edward Jones. "With Roundup Ready, it's fairly simple. We don't even have to work the soil. We just go plant right behind the combine."

The Roundup Ready gene is a boon, but there's a lot more breeding that goes into the beans that Morse grows. Decades before the herbicide-resistant beans became available, plant geneticists, including MU's Dave Sleper, began testing as many as 1,000 experimental varieties of soybeans a year to develop lines that thrive in Missouri's particular combination of heat, humidity, rainfall, soils and pests. "Now, we handle an awful lot of junk," Sleper says. "But we must look at them all before eliminating any." In any given year, about 70 of those initial thousand or so varieties show enough promise to grow again. By the third generation, fewer than 10 remain, of which one or two eventually become available to farmers after further years of testing.

With the help of molecular mapping of soybeans, geneticists in Sleper's lab can streamline breeding by looking into individual plants' DNA for desirable traits. For instance, they can identify varieties that resist pests, such as soybean cyst nematodes, which devastate roots. Geneticists also can modify beans to yield healthier fats, more protein and more isoflavones, the compounds in soybeans believed to have cancer-fighting properties. These changes make the crop more healthful for consumers and valuable to farmers.

Good breeding goes a long way, but farmers must spray herbicides at the right time to get the biggest bang from their herbicide-resistant beans. MU's Bill Johnson researches the best application schedules. "There are better times than others to spray weeds," Johnson says. "Many farmers like to see clean fields in late July and early August, so they will spray later than they should. The reality is that they should spray earlier because the late weeds cause less yield penalty than if they have more weeds earlier." Johnson says his protocols are especially important in northern Missouri, where the shorter growing season allows soybeans less time to recover from weed competition.

— *Dale Smith*

In addition to his job as an investment broker, Scott Morse of Harrisonville, Mo., farms 55 acres of soybeans. He is shown here in his recently harvested field of wheat, which he has already planted with soybeans. Morse finds the new genetically modified bean varieties easy to use.