THE Stowers REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH

We're Open!!

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Almost three years to the day after Halloween in 1997, when construction planning began, the Stowers Institute for Medical Research opened the doors of its research facilities to the first scientists recruited to carry out the vision of Jim and Virginia Stowers to create the world's finest biomedical research facility. Led by Robb Krumlauf, Scientific Director, research teams moved into four laboratory suites on the second floor of the research building. They came from as far as London and China, also from Seattle, Chapel Hill, New York, Baltimore and Pasadena. They shipped valuable fruit flies and frozen mouse embryos and countless other things to allow them to maintain continuity in research projects that are intended to open the way to understanding some of the worst diseases we face.

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ALSO . . .

The Stowers Institute has received neighborly help from area research and educational institutions in getting off the ground and looks to them for cooperation in research efforts from which all can benefit.

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Dr. Richard D. Klausner, director of the National Cancer Institute, launches the Wednesday seminar series of the Stowers Institute and inaugurates auditorium designed with every conceivable audio-visual need in mind.

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Stowers Adventure Draws from Afar

From China and London they came, from New York and Seattle and Chapel Hill, and elsewhere – to carry out the vision of Jim and Virginia Stowers to create the best biomedical research facility in the world. The first week of November, the Stowers Institute for Medical Research opened the doors of its laboratory buildings to scientists and associates for what Bill Neaves, President and CEO, described as "the adventure on which we're about to embark."

"Jim and Virginia wanted to create the optimal environment for excellent science to occur," he told those joining together as the Stowers team, adding that the decision of Mr. and Mrs. Stowers to focus the research of the Institute on the regulation of the body's genes and proteins was "an extremely enlightened perspective" that could lead to major breakthroughs in medical care over the long term. "We are privileged to be in the position of implementing the vision they have articulated," he said.

Jim Stowers' words for the occasion were brief. "This Institute is not going to be the greatest if we don't attract the best scientists," he told the newcomers. "That's why we want you here."

Double Helix Sculpture

As they spoke, craftsmen in a workshop across town were welding and grinding to complete the 32-foot double helix sculpture that would be installed amidst the gardens and fountains, conveying the Stowers Institute's message of hope to all who pass by the campus at 50th and Rockhill Road in Kansas City.

The scientific teams, plus expanded administrative and facilities management teams – bringing the total to 53 Stowers members – went through three days of orientation Nov. 1-3 before getting access to their workspaces on Nov. 6.

Although a formal celebration of the completion of the Institute is planned in the spring, the first week of November was a long-anticipated inaugural for those who will do the work of the Institute. In the days and weeks leading up to the occupation of the research facilities, while construction crews were still polishing the floors and landscaping the $200 million complex, the countless things that make scientific research happen were beginning to come together, both on and off the site.

A Robot for the Dirty Work

There was the matter of installing and testing the Automated Cage and Rack Washing System – in simpler English a robotic system for washing mouse cages and replacing the bedding periodically, then returning the cages to their quarters without dirtying human hands. The first headache, however, was getting the $1.5 million, Swedish-built apparatus through U.S. Customs, which did not know what all the pieces were.

This caused a delay of five weeks in getting what some scientists call the "Mouse House" functional. It was probably what Kieran Pemberton, who came from London to continue his work on molecular events associated with leukemia with Leanne Wiedemann, meant by having "just a few teething problems."

Jeff Johnson, construction project manager, said the Stowers Institute was the first institution in the United States to install the robotic system, which is made by the Swedish firm Detach, a subsidiary of Steris Amsco.

Another element of the Stowers campus with a history and purpose as singular as that of the robotic wash system is the double helix sculpture on the terraced area just outside the main entrance to the research building. Larry Young, a sculptor in Columbia, Mo., designed the helix as a 22-inch bronze model, then computer technology was used to expand it to the dimensions and details of the 32-foot version for installation on the campus.

Then, artisans at A. Zahner Co., which executes artistic designs in metal, went to work to build the helix – weighing 11,000 pounds – out of 3/8-inch-thick stainless steel plate, grinding into the metal a finish of scrolled figure eights that the 10 spotlights pick up.

Trying Out the Mouse House

Before the high-valued transgenic mice of Robb Krumlauf, Scientific Director, could be shipped from his previous lab

Unpacking in the lab of Robb Krumlauf after the move from London. From left: Debra Ellies, Leanne Wiedemann, Dr. Krumlauf.

in London, "sentinel" mice from a lab in Massachusetts tested the animal quarters for several weeks for sanitary conditions and appropriateness for breeding. After they were sent to the University of Missouri at Columbia and tested for pathogens, both the facilities and the mice were found free of diseases, infections and contamination.

For Heather Marshall, the all-around second-in-command in Dr. Krumlauf's lab, preparation for the move from London to Kansas City really began nearly a year ago, soon after Dr. Krumlauf returned from his first visit to Kansas City full of enthusiasm for this effort to launch an entirely new research institute with the unabashed goal of becoming the very best. He wanted to accept the position he had been offered, he told her, but only if she would come also. That also meant Dr. Pemberton, to whom she is married, and their toddler daughter, Niahm (That's Irish and pronounced Neve). So the Marshall-Pemberton family made an inspection trip to Kansas City more than a year ago and concluded that they were ready to give the New World a try.

Once back in London, Dr. Marshall set about thawing and testing the mouse embryos she had been freezing for years because she is, above all, an expert in transgenic mice – the carefully bred mice on which Dr. Krumlauf depends for his research into molecular pathways that regulate how the head, brain and nervous system of mammals are built.

There was no intention to ship live mice across the Atlantic, rather to ship embryos and sperm and breed new mice here with the inherited characteristics of the mice on which Dr. Krumlauf has been working. Before shipping the embryos, Dr. Marshall wanted to make sure they were viable. "Most came out okay," she said, "except for two lines, and for those we can go back to the original samples and DNA and make them again."

Half of the sperm and embryos would be shipped on dry ice just in time to get into the facility. The rest was left behind in London in case something happened to the first shipment en route. Like other scientists, she doesn't want to think about the possibility of losing her supply of research animals.

Flies Make a Career

Or as Ting Xie said, "If my flies get killed, that's my career." Dr. Xie, who heads another of the independent Stowers laboratories, has been doing notable work in genetic and molecular analysis of stem cells and germ cell development, using *drosophila*, or fruit flies. He moved to Kansas City last winter from his previous post at the Carnegie Institution in Baltimore and occupied leased laboratory space across the street in the biological sciences complex of UMKC.

Preparing to make the move into the new Stowers labs, he planned to move a few vials at a time and test the environment. For his flies, this would be the second move in less than a year, and he didn't want to run the risk that the new facilities might hold unusual smells or other things that the flies might not tolerate.

continued next page

Photos: Don Ipock

***Heather Marshall** tests the reserve tank of liquid nitrogen that she uses to freeze mouse embryos.*

*Preparing to work in the lab of Linheng Li. From left: **CiCi He, Chao Niu, Jiwang Zhang.***

But nobody could be giving more thought to keeping fruit flies contented than Cliff Sonnenbrot, who was hired away from the Howard Hughes Medical

Photo: Don Ipock

Jeff Johnson, construction project manager, at the window of the library of the Stowers Institute.

Institute at Rockefeller University in New York. His full title at Stowers is Director, Central Support Facility/ Glasswash, Tissue Culture & Media Preparation. "Media," for some reason – and probably to the surprise of television pundits – is the term for fly food.

Almost as soon as he arrived in Kansas City in August and was assigned a temporary office in the Stowers administration building, Mr. Sonnenbrot, who has a master's degree in chemistry from Hunter College, started studying catalogues for the supplies to be ordered and figuring out how to launch his feeding operation in this brand-new place. He calculated that he would need 40 gallons of mixture a week to feed 6-7 million flies.

His recipe is basically yeast, cornmeal, agar and molasses. He uses a 60-gallon kettle to boil it, then cools the mixture and puts it into vials with a robotic dispensing system that he pioneered 10 years ago. Although all of the commands go through a computer, Mr. Sonnenbrot says that after doing this for 24 years he has "a lot of confidence in myself that I can do it blindly."

Searching for Post Docs

To those launching laboratories here, the challenge is great – and also exciting. Dr. Xie, though born and reared on a farm in China, came here from the U.S. East Coast and seemed keenly aware of the challenge he faced, for example, in attracting the high-quality post-doctoral research associates so crucial to the success of a laboratory, and of its leader.

The East and West Coasts, he said, get 90 percent of the first-rate, American-educated post docs because scientists starting out favor labs with reputations that will help their careers. He also noted that American universities do not produce enough people planning to go into research science, so the supply of post docs is limited. "Reality," he said, "is that only 55 percent of post docs we need in science come out of U.S. universities; the rest come from abroad."

"The Stowers Institute is just getting started," he added, "and it takes time to build our reputation. We have to publish articles in leading scientific journals about our research and make the Institute visible." Dr. Xie, in fact, has already shown his potential with a recent well-received report in *Science* magazine, the Bible of American scientists, about his research at Carnegie demonstrating that neighboring cells often tell stem cells what to do.

Despite the hurdles, he said, "I came to Stowers as a better opportunity to develop my career and to do science the way I want to do it. I want to do quality science, not just science."

That's just what Jim and Virginia Stowers want to hear.

> *"I came to Stowers as a better opportunity to develop my career and to do science the way I want to do it. I want to do quality science, not just science."*

Photo: Don Ipock

Mike Newhouse, information technology systems manager, checks out the rear-projection screens of the Stowers Institute auditorium.

DAY CARE TO BRAIN IMAGING

Stowers Institute Counts on Collaboration

In the three years since the Stowers Institute began construction and started the search for scientists to carry out its research vision, it has turned with growing frequency to larger, more established institutions in the Kansas City area for help in things as basic as child care and veterinary medicine and for potential cooperation in the loftiest of research goals.

When the University of Kansas Medical Center, for example, unveiled plans in October for a new brain imaging center, the Med Center's vice chancellor of research, Michael Welch, painted a vision of how such collaboration would enhance Kansas City's effort to become a center of life sciences research. He suggested that the imaging center, after it opens in 2002, might be the place to which Robb Krumlauf, the new scientific director of the Stowers Institute, sends his transgenic mice for imaging as part of his research into the molecular pathways that regulate development of the head, brain and nervous system.

In other words, send the mice a few dozen blocks across town in Kansas City instead of to California.

Dr. Welch's collaborative vision is one that is strongly shared by the Stowers Institute as it opens its doors to scientific research. For the four scientific teams that occupied the first laboratories in the research building on the Stowers campus at the beginning of November, nearby institutions have been a neighborly shoulder to lean on.

Neighborly Help from UMKC

The University of Missouri-Kansas City, just across the street, resolved the child care problem for some Stowers scientists by giving them access to the university's well-regarded Berkley Child and Family Development Center. When one of the four lab heads, Ting Xie, had to move from his old institution in Baltimore months ahead of completion of his Stowers lab, the Institute was able to lease lab space for him from UMKC.

Midwest Research Institute, just down the street from Stowers, provided safety training for all laboratory personnel. And when the Stowers Institute found a scientist whom it especially wanted to recruit, and the scientist also wanted a tenured appointment at the University of Kansas, KU Chancellor Robert Hemenway arranged for the scientist to present his research to KU scientists – a way for them to assess his potential for KU appointment.

In the near future, these connections could advance well beyond such nuts and bolts questions. That was the message William B. Neaves, President and CEO of the Stowers Institute, took to Chicago recently for a meeting of the Association of American Medical Colleges, where he described the way scientific collaborations might proceed.

He said that the major contribution the Stowers Institute can make to the collaborative effort at this point will be its expertise in discovery science aimed at identifying genes and proteins that control fundamental processes in living cells.

Strength in Discovery

Stowers scientists will, from time to time, uncover proteins that represent potential targets for new therapeutic approaches to the prevention of disease. When this happens, the Stowers scientist will want to collaborate with colleagues who have expertise in proteomics, the field of research into the body's proteins that follows on the heels of the Human Genome Project.

After discovering a protein that might be a good target for a new drug, the three-dimensional structure of its chain of amino acids must be determined; then drugs can be developed to interact with the protein in the treatment of disease. He gave the following example of how that might occur:

"Across the street, UMKC has a group of scientists who are skilled at using x-ray crystallography to determine the atomic structure of large and complex proteins. What we can offer in return is a regular flow of newly discovered proteins. We have the ability to discover proteins of biological and medical importance, and they have the ability to discern the structure of these proteins."

"Once we know the three-dimensional atomic structure of the protein," Dr. Neaves continued, "we could turn to the Higuchi Biosciences Center at KU, which has experience in designing small molecules to interact with a medically important protein in a way that will yield the desired outcome."

Toxicity Tests and Clinical Tryouts

As knowledge about this particular protein moves along the research chain, investigators at Midwest Research Institute might conceivably test the new drug's toxicity, and researchers in physiology at KU Med Center might explore the systemic effects in whole animals. Eventually, clinical colleagues at Children's Mercy Hospital or at another institution engaging in human subject research might begin phase one testing of the new drug in humans.

"The Stowers Institute is highly motivated to engage in these collaborations," said Dr. Neaves. "We don't want to spend scarce research dollars to duplicate the basic and preclinical work of others, and we don't have the staff or facilities for clinical investigation. We need colleagues and collaborators in our neighboring institutions to do those things we are unable to do ourselves and to enable us to focus on what we do best."

Mortgages and Commutes: How We Seem to Others

Heather Marshall and Kieran Pemberton found the house of their dreams in Shawnee, Kansas, via the magic of the Internet from their old home in London, but when they arrived in Kansas City to take up their research positions with the Stowers Institute they discovered that the same computer wizardry could obstinately say no to their mortgage request.

Drawing people from around the globe and across the country to launch an ambitious biomedical research facility, the Stowers Institute has found that Kansas City's charm attracts, as does the glistening wonder of a new research center.

Chao Niu and Jiwang Zhang, still groggy after long flights from China to join the Stowers scientific team as post-doctoral associates, found their housing choices limited by the fact that they don't either one know how to drive. In a town where public transportation is iffy and where people haven't much taken to commuting by bicycle, Drs. Niu and Zhang were elated to learn a few days after their arrival that two apartments were available a few blocks from the Institute.

Still ahead were such concerns as how to find groceries in the midtown neighborhood around the Stowers Institute – with only limited English and ready smiles at their command.

City's Charm Attracts

Drawing people from around the globe and across the country to launch an ambitious biomedical research facility, the Stowers Institute has found that Kansas City's charm attracts, as does the glistening wonder of a new research center. Jim Coffman, for instance, fell in love with, and bought, one of the old stone houses at 47th and Holmes. He was happy to report that he could walk from there to his laboratory in less time than his former commute had been in Southern California traffic.

For most of the new arrivals, there are also matters like the tight housing market and ever-rising real estate prices, the shortage of day care and public transportation, and the intricacies of finding good schools for children.

Ting Xie, who moved his research to Kansas City from the Carnegie Institution in Baltimore earlier this year and set up a temporary lab at the University of Missouri-Kansas City until the Institute was completed, said the quality of education available for their two pre-school-age sons is uppermost in the minds of him and his wife as they look for permanent housing.

"We Chinese always put the education of our children first," he said.

By contrast, some problems and cultural differences seem quite manageable – for instance, the "gravy nodules" that make dinner an easier task in England but are not to be found in the sprawling supermarkets of Johnson County. Dr. Marshall plans to resolve that issue by having her mother bring a good supply of the nodules when she comes for Christmas.

When Dr. Marshall and her husband, Dr. Pemberton, made the decision a year ago to make the move to Kansas City, he quickly turned to the Internet to start house hunting from 4,000 miles away. There, he found a house plan that was especially appealing, which was being built by a developer in the southeastern part of Johnson County. When they arrived in Kansas City, however, they learned that the developer was no longer building that model in that particular location, but was building it in a new area in the more northwestern part of the county. Within a week they had settled on their Shawnee house, which was still under construction.

Mortgage Elusive

Then came the matter of a mortgage. The small, friendly midtown bank where they had opened their account tried – but failed – to get mortgage approval after feeding their financial data into the computer. They eventually found a mortgage, at an attractive interest rate, from a big savings and loan with the apparent clout to make a decision independent of the computer, but the warning they had for others is that computer credit analysis programs have been slow to join the trend toward globalization.

Even Chicago-born Leanne Wiedemann, coming home after 14 years abroad, discovered that having an American Express card issued in Britain instead of a U.S.-issued card produced a rude response to her first attempts to get local credit. "No Credit History," the computer spit back. However, a handsome profit from the sale of their London home helped cushion her and her husband, Robb Krumlauf, the Institute's new scientific director, as they settled into the home they bought in Kansas City.

There was, however, one matter that computers could neither resolve nor mess up: What was the appropriate amount to spend on the gift for their eight-year-old to take to a birthday party?

Top Cancer Expert Launches Seminar

The honor of launching the Stowers Institute's Wednesday seminar series – and inaugurating a 225-seat auditorium loaded with every conceivable audiovisual marvel – fell to the man often described as the nation's foremost cancer authority, Dr. Richard D. Klausner, director of the National Cancer Institute.

Photo: Don Ipock

Gathered in the Stowers Institute auditorium after a seminar by Richard D. Klausner, director of the National Cancer Institute, from left: U.S. Sen. Sam Brownback of Kansas, Stowers President and CEO Bill Neaves, Scientific Director Robb Krumlauf, and Dr. Klausner.

"I really don't think you had to fix the place up this much for me," he joked as he stood at the podium before about 150 area scientists and physicians to begin an hour-long lecture on his own research into the VHL tumor suppressor gene.

"I suspect that this building is going to ease your recruitment efforts," he assured leaders of the Stowers Institute, "or else you will have more speakers who find it hard to go home."

The auditorium, on the ground level of the Stowers Institute research complex, which was occupied by scientists a few days before the Klausner speech, is designed to provide the ultimate in comfort and technology for scientific gatherings. That includes a variety of projection screens for the use of slides and CDs, fine wood paneling, soft lighting from the sides and ceiling and near-perfect acoustics.

Although, when Dr. Klausner looked for a pointer as he talked about the data in his slides, he found none on the podium. "This place doesn't have everything," he commented as someone in the audience produced one.

The matter of a pointer was apparently overlooked in the rush to have the auditorium ready for the Klausner appearance. Mike Newhouse, information technology systems manager, and Robb Krumlauf, scientific director, had put the audio-visual equipment through its paces just the day before, one day after construction workers pulled out of the facility.

Dr. Klausner's seminar appearance ended a day in which he was the main speaker at the annual luncheon of the Kansas City Area Development Council at the Muehlebach Hotel, where Jim and Virginia Stowers were honored for their contribution to creating a biomedical research community in Kansas City. At the same time, the Stowers Institute legal counsel, David A. Welte, partner in the law firm Polsinelli, Shalton & Welte, took office as co-chair of the KCADC. The Development Council is the partner of the Civic Council of Greater Kansas City in launching the area-wide initiative with the goal of making Kansas City a major national player in life sciences research and biotechnology.

U.S. Sen. Sam Brownback of Kansas, who arranged for Dr. Klausner's visit to the area and attended both the luncheon and the seminar, described the Stowers Institute as the anchor of that effort and promised to continue lending support from his position in Washington.

*Hope Shares*SM

Contributions of at least $1,000 have been received from the following individuals, businesses and foundations since August 1, 2000.

INDIVIDUALS:

Malcolm M. and Kathy B. Aslin, Shawnee Mission, Kan.
E. Lois and Gilbert Cole, Kansas City, Mo.
David L. and Nancy J. Dilley, Leawood, Kan.
Samuel D. and Melody Goller, Leawood, Kan.
Martha G. and Mark Miller, Overland Park, Kan.
Amy L. Noelker, Blue Springs, Mo.
Jody Anne Varner, Sausalito, Calif.

FOUNDATIONS and BUSINESSES:

Sprint Corp. Charity Golf Classic

Thank You for These Gifts of Hope

For this, you will never be forgotten

Every attempt has been made to assure the accuracy of the above list. We believe that all gifts of at least $1,000 since Aug. 1, 2000, have been included. In case of error or omission the Stowers Institute wishes to be advised.

Craftsmen worked to assemble the 32-foot double helix sculpture before installing it as a centerpiece of the Stowers campus.

Photo courtesy A. Zahner Co.

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