THE Stowers REPORT

NEWS AND INSIGHT FROM THE STOWERS INSTITUTE FOR MEDICAL RESEARCH

Bringing to Life The Stowers Institute

From the time Troy Jarman, labor foreman, opens the gates of the construction site before dawn every work day, a longstanding relationship of trust makes the gritty work of building the Stowers Institute more than just a job. That feeling begins with the friendship that developed years ago between Jim Stowers, president of the Institute, and Rick Fortner, general superintendent of the project for J.E. Dunn, the principal contractor. It extends through layer after layer of craftsmen and subcontractors among the more than 400 men and women at work on the job site.

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ISSUE 1

INSIDE ...

Robert E. Krumlauf

Scientific Director Coming Home from England With Confidence and Spirit of Collaboration

Dr. Robb Krumlauf

Robb Krumlauf's working life began along a path that satisfied his father, who wanted him to have a "real job." He majored in chemical engineering at Vanderbilt, then went to work in a lab for Stokley Van Camp Inc., trying to figure out ways to put together medicines for long-term release in the body.

But a tremendous thirst for more knowledge soon drove him back to the classroom at Ohio State University. At first, he studied without great design, except to answer the jumble of questions in his mind – such as, what makes an arm different from a leg? He took course after course while continuing his work in the Stokley Van Camp lab in Columbus. At the urging of professors, he eventually joined a doctoral program with fellowship support from the National Institutes of Health. Out of that experience emerged Robert E. Krumlauf, Ph.D. in Developmental Biology.

Now, 20 years later, he has been named scientific director of the Stowers Institute, which found in him the qualities needed to lead a facility that aspires to conduct basic research that will facilitate breakthroughs in the cure or prevention of devastating diseases with genetic bases. Dr. Krumlauf's career has embraced many of the components of the Stowers Institute vision, including: multidisciplinary work involving scientists of many specialties and with the door always open to collaborate with clinical researchers seeking to turn results of basic research into treatments and technologies.

Under Dr. Krumlauf's leadership, the first group of scientists and their associates will set up research at the Stowers Institute when the first laboratory building is completed and ready for use toward the end of 2000.

Though a native Midwesterner, he brings to the Stowers Institute 14 years' experience with England's National Institute for Medical Research at Mill Hill, London, the last nine years as head of the Division of Developmental Neurobiology. Before going to Mill Hill, Dr. Krumlauf did postdoctoral training at the Fox Chase Institute for Cancer Research in Philadelphia and the Beatson Institute for Cancer Research in Glasgow, Scotland.

His research and choices of places to study and work reveal something about the value he places on collaboration and interaction among scientists because, as he says, "we never know where the next big idea will come from."

As a graduate student, he worked on the genetics of fungi – trying to use genetics to understand relationships between things in the body and asking whether mutants or mutations could help us understand how things were normally supposed to be. When it came time to do postdoctoral training he wanted to do something that would bring his research closer to human or mammalian problems. An excellent cancer research center in Glasgow – together with the chance to pursue his mountaineering interests in the Scottish hills – drew him across the Atlantic.

In Glasgow, he did some of the earliest work in sorting human chromosomes based on size and preparing genomic libraries – methods that are now routinely used in genome research projects. But he eventually became frustrated with the lack of clinical connections, feeling that access to patient material might help his research. He also sensed a critical need for model systems on which to study human problems and diseases. So, he and his wife, Leanne Wiedemann, a research scientist with a substantial record in studying the molecular bases of leukemias, chose to do their next postdocs in Philadelphia, where the Fox Chase Institute combined basic and clinical research with a hospital community.

Working with the imminent biologist Shirley Tilghman on how mouse genes were regulated for development, Dr. Krumlauf did research in Philadelphia that put him on the cutting edge of the developing technique for inserting genes into the germ line of mice. This was a breakthrough toward use of mice as a model system for studying fundamental problems of biology.

From Philadelphia, he became a regular on the international circuit of conferences and seminars that are so important to scientists for generating and exchanging ideas and talking about research results. "I felt that I needed to

understand more about mice and how the mouse embryo developed and as I traveled I began to realize that about 75 or 80 percent of the best mouse embryologists in the world were concentrated in a small area of the United Kingdom between London, Cambridge and Oxford."

His discussions and contacts with those embryologists eventually led to an invitation to join the government-funded National Institute for Medical Research, often known by its location – Mill Hill. Beginning as group leader in the Laboratory of Eukaryotic Molecular Genetics, he later added work as an adjunct research fellow at University College London and in 1991 became Head of Division of Developmental Neurobiology at Mill Hill.

At Mill Hill, fellow scientists told him that the important thing was to do interesting things. It is fine to publish only a small number of papers, they said, but the most important thing is to do interesting things and ask important questions.

"This encouraged me to take gambles, to do many speculative things," he said. "It's important to have faith in the people around you and know that they will support you even through hard times. This is essential because most of what scientists try doesn't work or, when we test something, it yields unexpected answers and we can't understand why. The gems of excitement that we get from time to time are few and far between. We have to live on them for years afterward. If you have to fight your colleagues it's worse."

At Mill Hill, his international stature grew substantially. While focusing on the mouse for his research, he developed a rare understanding of many other model systems as well – fruit flies, puffer fish, chickens and frogs. Focusing his research on the roles of the *Hox* genes in development of the nervous system in vertebrates, he has become strongly convinced of the value that the study of many different animals and organisms has for learning about the workings of the human body.

"The average person might wonder why, if we want to learn about humans, would we be interested in studying frogs, fish, flies or worms," he said. "Yet, what I can tell you is that some of the most instrumental landmark findings in shaping medical research have come directly from unexpected findings in those animal systems."

As examples, he cited the work of another scientist on *Drosophila* – the fruit fly – that led to discovery of a gene that is now a major target in basal cell carcinomas and a number of other human diseases. And of other scientists whose work on the worm known as *c. elegans* led to the finding that at least some cancers grow because of the failure of a gene that should tell cells when to die.

"This has provided tremendous insight into clinical and therapeutic approaches to cancer," he said, "but nobody would have thought of starting that research by studying the worm. You never know where the knowledge will come from."

"We're going through a revolution in biology and medicine where people say, 'I'm interested in this problem, but maybe I should study it in different model systems and then find a very rapid way to confirm that this is relevant for human genetic disease.' No one really has expertise in all these areas, and this is why we have to draw on broader bases of collaboration within the scientific community. So, people working on flies will collaborate with those working on humans and vice versa. It's a very stimulating environment because people are very interested in what their colleagues are doing and appreciate that just around the corner something could pop up that they've been looking for all their lives."

Dr. Krumlauf said he feels lucky to be part of a community that works well together in London and expects to see some of the same ways of working develop at the Stowers Institute.

"Part of my interest in coming to Stowers is the opportunity to be part of an enterprise that wants to integrate a number of different approaches and technologies, to work in a collaborative way, and to do this in a fun environment. This is very appealing to me. I hope I can bring to the Institute some of the advantages and ideas that we have at Mill Hill."

He and his wife are also drawn by the desire to come home to America, and the Midwest particularly, which enables them and their seven-year-old son, Matthew, to be closer to family in Ohio and Chicago. But there's one little piece of England that they're planning to hold onto – the canal boat in which they share ownership with three other families.

They use the 60-foot-long boat, equipped with beds and bunks, for lazy trips through the idyllic English countryside, traveling on the several thousand miles of canals that were built at the time of the Industrial Revolution to transport goods and services. The boats were originally drawn along the narrow canals by horses on the shore; today, they're powered by diesel.

"In science, everything is done so fast," he said, "so it is a pleasant switch to find ourselves on a boat where we can't go more than three miles an hour – people walking can go faster than that. You run the locks yourself; there are pubs in the countryside and it's very rural, but you also go through small cities. It's almost like experiencing industrial history. We'd be loath to let it go."

Relationship of Trust Behind Steel

Like most great things, it began as a dream, and the man with the dream told another man about it. Thus began the trusting relationship that lies behind the day-by-day, steel-and-concrete, nuts-and-bolts work of bringing the Stowers Institute to life.

***Rick Fortner**, general superintendent on the Stowers Institute construction site, began a trusting relationship with Jim Stowers years ago. "We became friends … and he began to tell me about his dream, and his dream was the Stowers Institute."*

As Rick Fortner remembers the beginning of his friendship with Jim Stowers, the two of them encountered each other while walking around the construction site for the second of the two office towers in Kansas City that house American Century, the Stowers family's mutual funds company. It was a Friday afternoon seven or eight years ago. Mr. Fortner was job superintendent for J. E. Dunn Construction Co., the general contractor.

"Mr. Stowers introduced himself, and I introduced myself," Mr. Fortner recalled, "and I asked if he would be interested in going on a job tour. For about 45 minutes we walked around, and he asked questions. From that day on, it became a Friday afternoon ritual. I think he loves construction.

"We became friends, and as we moved along in that project and had more meetings he began to tell me about his dream, and his dream was the Stowers Institute. We kind of parted with the understanding that when it was ready to become a reality he would call me. And that's what he did."

With the J.E. Dunn firm again selected as general contractor, Rick Fortner became general superintendent for construction of the Stowers Institute in the summer of 1998. He came straight from building the new federal courthouse in downtown Kansas City, a challenging radial structure with pie-shaped courtrooms looking out to the Missouri River.

The Dunn firm is a construction powerhouse, with revenues that approached $1 billion in 1998. Its bright blue cranes reign high in the sky over many building sites in these booming times, including that of the Sprint Corp. campus in suburban Overland Park, the largest corporate construction project anywhere in the country. Rick Fortner's own resume also includes the soaring temple of the national headquarters of the Reorganized Church of Latter Day Saints in Independence, Mo., and a sprawling commercial project in Tulsa.

***Troy Jarman**, left, and **Doug Seiter** work side-by-side as members of what they like to call the A-Team, running the grubby, daily cement pours required to build the Stowers Institute.*

The trust that developed between him and Jim Stowers during the American Century job is repeated again and again through the long days that go into building the 600,000-square-foot Stowers Institute. It carries over into the relationships between Rick Fortner and the some 400 people scattered all over the job site – many of whom have worked with him on other jobs – and among the vast network of subcontractors representing many construction trades who work with the Dunn firm.

Their work begins at 7 a.m. in the summer, 7:30 in the winter. Labor foreman Troy Jarman is on the scene well before that. He leaves his home in the countryside outside Raymore, Mo.,

> *"I think we're going to be top class … We're doing it one time and doing it right."*

and Concrete of Stowers Institute

while it's still dark and drives into the city in time to open the gates to the work site about 5:45 a.m. Small and wiry, he'll probably walk 20 miles on the job site in the course of the day, up and down, back and forth.

Craftsmen, angling for a good parking spot in the busy midtown neighborhood, begin to arrive shortly after Mr. Jarman. They sit in their cars and pickups with country music playing, and drink coffee and talk until it's time to go to work.

Timothee Richardson, a laborer who usually gets to work a few minutes after Mr. Jarman, quickly starts one of her regular tasks – putting jugs of water and Gatorade around at all the work locations on the 10-acre site.

***Timothee Richardson**, a laborer, puts first priority on keeping the more than 400 craftsmen supplied with water and Gatorade. "At first, the guys thought, How is she going to make it in work boots?"*

"Some may think I'm doing a light job," she said, "but water is the first priority on this job – making sure everybody has liquids."

Fifteen years ago, Mrs. Richardson – she's called Timmie all over the site – decided to "get out of pantyhose and do something different." She was then selling jewelry, and the something different she chose was construction.

"At first, it was difficult," she said. "The guys thought, 'She's come from air conditioning and high heels, so how are we to know she's going to make it in work boots?'"

Since then she has shown she has muscles enough to swing a sledge hammer in demolition and nerve enough to wield cutting torches. She often works on the cleanup after Troy Jarman and his crew complete their daily cement pours – creating the walls, decks and pillars that form the structure of the Stowers Institute.

Because the Stowers Institute is being built in about half the time normally required for a scientific research facility, the construction schedule is laid out like five concurrent projects. That means many different tasks at different levels of construction are being done at the same time in the five buildings that will comprise the Institute. Mike Householder, senior project manager for Dunn, and Mr. Fortner coordinate with Jeff Johnson, project manager on behalf of the Stowers Institute.

There are five labor foremen and crews on the site, but Mr. Jarman's group – with a touch of bravura – has assumed for itself the title of the A-Team. Why? Maybe, as Mrs. Richardson says, it's because they keep each other going even when it's too hot or too cold and when their bodies are feeling their ages. Or maybe it's the corny tricks they play on themselves and others – like pouring a bucket of water on a couple of carpenters down in a hole, then pretending to have no idea who did it.

It may also be – as Doug Seiter, Mr. Jarman's right-hand man, suggests – the way the A-Team races to stay ahead of the turquoise and white trucks from Fordyce Concrete Co. that come and go throughout most of every working day. Each carries 10 cubic yards of cement. Carpenters lay the forms, and Mr. Jarman's crew, usually nine men, does the pouring and smoothing.

"We poured 470 yards one day," said Mr. Seiter. "That's 47 trucks loaded with cement. We go faster than they can get it here. But we still have a good time."

"We lose very little time from bad weather," Mr. Jarman said. "If it's below 32 degrees and not climbing, we don't pour, but we had hardly any weather like that last winter."

Even the record setting heat wave of the summer of '99 – with day after day of temperatures topping 100 degrees in Kansas City – didn't slow the work. "The heat makes the cement set quicker," Mr. Jarman said.

As for rain – "We say it never rains on a Dunn job," Mr. Seiter said.

While the A-team can rightfully claim to be doing a huge amount of work to create the basic structures of the Stowers Institute, Ed Hale says – with a pipefitter's pride – that the complex

***Ed Hale**, left, and **Paul Smith** of A.D. Jacobson Co., the mechanical contractor. Mr. Hale calls the pipefitters' work "the heartbeat of the buildings." To Mr. Smith, it's the "circulatory system."*

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***Jack Searcy** of Cates Sheet Metal, which does the big ductwork, stands just slightly taller, at 6 feet 6, than the width of some of that ductwork.*

would be little more than a lifeless mass of concrete and steel without the ductwork and piping that his people are putting into the buildings.

"I refer to our system as the heart-beat of the buildings," said Mr. Hale, who is general foreman of the pipefitters. "We supply the air – the life-support system – for the research mice, to be certain they have proper air and humidity and that the air is not cross-contaminated."

Mr. Hale works for A. D. Jacobson Co., the mechanical contractor. Among other things, the firm is installing 25 to 30 miles of pipe to carry air or water – pipes that range from a pneumatic control tube just one-eighth of an inch in diameter up to some pipes that are 24 inches in diameter.

"The HVAC system – heating, ventilation and air conditioning – is like the circulatory system of a body," explained Paul Smith, project manager on the site for A. D. Jacobson.

Although A. D. Jacobson has been in business since 1919 and has worked on many major projects in Kansas City, this one is expected to be its largest ever in dollar terms. Mr. Smith gave some examples of what makes it so expensive:

- Chemical-resistant six-inch piping to carry away laboratory waste costs $138 a foot from the supplier – compared with $7-$8 for more typical piping.
- The central plant will have 3,550 tons of air conditioning, probably twice as much as required in an office building with the same square footage.
- There will be five steam boilers, two of which will be used primarily for cleaning mice cages and laboratory equipment.
- There will be underground storage for 30,000 gallons of fuel to operate the backup generators in case the regular supply of electricity or natural gas is interrupted – enough to keep the campus going for 60 hours at 60 percent of capacity. This assures that no research work will be lost and that animal-care facilities can continue to function normally.

***Gary Chumley**, coordinator for Broadway Electric, enjoys one of the few desk jobs on the construction site. "We're using the finest quality methods you can get on a facility this large."*

Jacobson has subcontracted the big ductwork to Cates Sheet Metal, whose field superintendent, Jack Searcy, stands – at 6 feet 6 – just slightly taller than the width of some of that ductwork. His dozen or so sheet metal workers are installing ducts as large as 72 inches by 60 inches with 4-inch insulated walls.

One of the features of the ductwork is that all of the insulation for the laboratory buildings is encased in Mylar, a polyester film that Mr. Searcy equates to "big Baggies." That is done "so the insulation can't break lose and get into the air flow in the labs," he said.

If the pipefitters and sheet metal workers are providing the circulation and respiratory systems of the Institute, then the energy to power those systems is made possible by the hands of 30-some electricians from Broadway Electric, another firm with a long association with the Dunn company and the Stowers family.

"This is my 11th or 12th year on a Stowers project. I'm almost a relative," said Gary Chumley, the on-site coordinator for Broadway Electric.

In addition to the obvious things – electric lines and lighting – Broadway Electric is providing fiber optics for voice and data transmission; the security system, including cameras and card keys; the environmental monitoring system; audio-visual and cable television networks, and – in another feature intended to protect research efforts – a system designed to protect all of the research and office facilities from lightning strikes.

"We're using the finest quality methods you can get on a facility this large," said Mr. Chumley. "The research community can be assured that everything is being done as it should be."

In superlatives, however, it is difficult to top the 200,000 pounds of ornamental stainless steel that Baker-Smith Sheet Metal is installing – comprising the roofing, flashings, architectural louvers and column covers of the five-building complex. Jerry Schaefer, one of the two owners of Baker-Smith, said his firm buys the metal

in 4-foot by 10-foot flat sheets, then handcrafts it in the firm's shops before delivering the metal for installation. Even the roof, which is made of glass-bead blasted stainless steel, is custom fabrication.

Stainless steel was chosen for the roof because it is highly resistant to corrosion and to any possible chemical. The glass bead processing removes the shine from the metal and leaves a matte finish. As the weather and sun change, the roof will take on the characteristics of the sky.

Jerry Schaefer *of Baker-Smith Sheet Metal, whose craftsmen are installing a stainless steel roof that "will look as good 50 years from now as when it's finished."*

"These buildings will be here for my lifetime, at least," said Mr. Schaefer, "and this roof will look as good 50 years from now as when it's finished."

Toward the end of 2000, when these and other craftsmen are finished and scientists are ready to move into the laboratories, responsibility for care and management of the gleaming facility will pass to Neil Krahn, facilities manager for the Stowers Institute. His skills at precision maintenance were honed in 14 years as an engineer aboard nuclear-powered submarines of the U.S. Navy, a job where any error could be deadly. Later, he added experience as plant operator and engineer for hospitals and colleges.

"I ran all the turbines and the pumps and anything mechanical on the submarine reactor," he said. "Air compressors, generators – all of that I learned in the Navy. I was born and raised on a farm in Wisconsin. All I knew was milking cows and driving a tractor until I joined the Navy in '64; next thing I knew I was riding a submarine."

Mr. Krahn, along with Mark Bearden, who will work with him in operating and maintaining the facility, was closely involved in planning the mechanical and electrical aspects of the Institute and has been alongside those building the Institute every day. "We reviewed all the prints," he said. "We told them which suppliers had good local reps. We looked at system designs. In the first cut, we recommended quite a few

Neil Krahn *left, will bring precision maintenance skills learned on Navy nuclear submarines to the care of the Stowers Institute facilities after the construction crews pack up and leave.* ***Mark Bearden****, right, works with him.*

changes. For instance, we told the architects that their calculations of outdoor temperatures didn't go high enough in the summer and low enough in the winter. We looked at the operation of the air handlers and boilers. Instead of automatic we wanted manual interface. We had pages and pages of questions and answers that we bandied back and forth."

"I think we're going to be top class," he said. "We're not going after an economy class structure. We're doing it one time and doing it right. Mr. Stowers has said that from the very beginning."

Working Conditions Gritty, Sense of Accomplishment High

The men and women building the Stowers Institute display the no-nonsense qualities of people who bring buildings into being. Theirs are gritty days of dust, mud, rain, snow, heat and cold, but they enjoy a great sense of accomplishment in being able to look around and say: I helped create that.

"You get very hot and very cold, but you can see what's done," says Troy Jarman.

Doug Seiter also appreciates the fact that the standing of laborers like him is improving a bit. "We used to be considered help from the neck down – no brains. But now we're considered more of a craftsman – not just a grunt and go-fer. They finally figured out we got a little piece of brain."

That he has both a brain and sensitivity is obvious in his after-hours, when he serves his religious faith as a clown minister. What began with occasional clowning at parties developed into something bigger after his minister suggested he attend a school for Christian clowning. Sometimes accompanied by his 11-year-old son, he does a hobo routine at prisons, revivals, vacation Bible schools, and elsewhere.

"I use illusions, like magic, to tell Bible stories," he said. "The story of Jesus getting crucified, for example. I have some playing cards with the face of Jesus on them; the point I make is that you're missing something from life if Jesus isn't there. And I tie balloons together and use them to tell the story of Jonah and the whale."

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Nelson R. Pleau

Administrative Chief Brings Hughes Background

It is a mark of the excitement generated in the scientific community by the creation of the Stowers Institute that Nelson R. Pleau left a senior administrative position with the Howard Hughes Medical Institute to join the Stowers Institute in its formative stage.

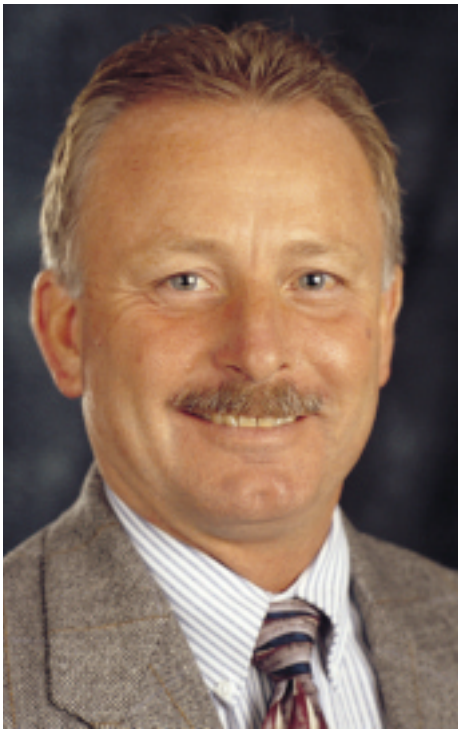
As chief administrative officer since November 1998, Mr. Pleau has taken a leading role in development of the Stowers laboratory facilities on the campus under construction in Kansas City. He is also coordinating recruitment of the first group of scientists to direct laboratories at the Institute when it opens its research facilities in late 2000.

Mr. Pleau brings to his position 14 years' experience in administration with the Hughes Institute, the largest private, nonprofit source of funding for biomedical research in the United States. He said he was drawn to the Stowers Institute by the quality of the facilities being created – almost unmatched in the scientific world – and by the personal commitment of Virginia and James E. Stowers Jr.

"What attracted me was the excitement about what the Stowers' are doing for the scientific community and for humanity," he said. "Not many research institutes have started with these kinds of resources. Commitment, facilities, and philosophies, both scientific and administrative, make the Stowers Institute a project second to none. There is nothing like this going on anywhere else and there hasn't been a project like this for the last 10 or 15 years."

"I looked at the potential and realized that this was where I wanted to be. Change, adventure and the challenge to help build and establish a world-class medical research institute were exciting and motivating forces that drove me here."

For 10 years, Mr. Pleau was manager of administrative services for Hughes-sponsored research facilities in four western states, working from offices in Salt Lake City. Earlier, he held similar responsibilities in the Boston office of the Hughes Institute, coordinating and supervising construction of new research space at Brigham and Women's Hospital, Harvard Medical School and Children's Hospital.



Nelson R. Pleau

Despite the prestige and immense resources of the Hughes Institute, Mr. Pleau said he had accepted the Stowers offer because he was beginning to feel professionally stagnated at Hughes. "It is so big now that it loses touch with its people," he said. "I like the family environment here."

Since joining the Stowers Institute, he said, he has taken a close look at the laboratory floor designs and made a few changes "to make the space more functional and allow for a variety of special procedure and core facilities."

"We have the opportunity to provide many state-of-the-art and advanced technologies to the research space," he said. "Core and special procedure facilities such as central glasswash, central computing, core centrifugation, tissue culture and sequencing are just a few. The 35,000-square-foot animal facility will certainly be one of the best designed in the country."

In the search for scientists, he is working closely with members of the Scientific Advisory Board and the Ad Hoc Review Committee, both made up of distinguished scientists.

"In just the last 8 to 10 months, especially due to our recruitment effort, the Stowers Institute has become a more recognized entity within the scientific community," he said. "The local academic research community and the biotechnology and pharmaceutical industries are very excited about the Institute. Over the next several years our research will provide the nucleus that will bring world recognition to the Institute, to Kansas City and to the entire Midwest."

"Change, adventure and the challenge to help build and establish a world-class medical research institute were exciting and motivating forces that drove me here."

Mr. Pleau grew up in Medway, Mass., as one of 10 children. After studying two years at Johnson and Wales University in Providence, R. I., his sense of adventure carried him from New England to New Mexico, where he earned a bachelor's degree in business administration from the College of Santa Fe. He later received an MBA from the University of Phoenix.

James A. Coffman, Linheng Li

First Stowers Lab Leaders Draw Praise, Encouragement From Distinguished Mentors

Two researchers now working in Stowers Institute consortia laboratories at Caltech and the University of Washington have been selected to join the Stowers Institute in Kansas City when laboratory facilities open toward the end of 2000. James A. Coffman, now at Caltech, and Linheng Li, now at the University of Washington, will direct their own laboratories at Stowers with the rank of assistant research scientists – roughly the equivalent of assistant professor in a university.

Drs. Coffman and Li, who were selected from among more than 100 scientists who responded to the initial call for applications by the Stowers Institute, will work with Dr. Robert E. Krumlauf, the newly appointed scientific director.

Both of them come with high recommendations from some of the country's top scientists, including Dr. Lee Hood and Dr. Eric Davidson, members of the Stowers Institute's Scientific Advisory Board. In particular, both have been cited for their abilities to develop new technologies and apply them to biological research. That is a key component of the scientific mission of the Stowers Institute.

"Jim is technologically excellent," said Dr. Davidson in recommending Dr. Coffman. "One of his major contributions here has been his development of a robotic technology for transcription factor purification by multiplexed affinity chromatography columns. But Jim is also a scholar, and a thoughtful developmental biologist."

Dr. Coffman was born in Arlington, Va., received his bachelor's degree in biology at Carleton College and his Ph.D. in zoology/cell and molecular biology from Duke University. He was a research assistant at Duke and at Woods Hole Marine Biological Laboratory, joining Caltech in 1990. Since 1997, he has been director of the Caltech Transcription Factor Research/Resource Center.

At Caltech, Dr. Coffman has been involved in the widely known research on sea urchin embryos by Dr. Davidson's lab. He played a major role in developing technology for analyzing the regulatory systems that control spatial patterns of gene expression in the sea urchin embryo.

Dr. Barbara Trask, vice chair of Dr. Hood's Molecular Biotechnology Department at the University of Washington School of Medicine, described Dr. Li as doing a "spectacular job" and as being "at the cutting edge of new technologies for molecular genetics and genome analysis. His technical contributions have been clever and expeditious."

Linheng Li was born in China but is now a U.S. citizen. He earned a bachelor's degree in biology and a master's degree in genetics at Fudan University in Shanghai before coming to the United States, then obtained a master's degree and Ph.D. in molecular and cellular biology at New York University Medical School.

He joined Dr. Hood's lab at the University of Washington in 1995 and in 1998 was promoted to affiliate assistant professor.

Built on the Desire to Offer Hope

- *Hope to people whose genes condemn them to a long battle with cancer.*
- *Hope to parents who wake in the night to tend a diabetic child, then toss and turn as they wonder what the future holds for their son or daughter.*
- *And hope to adult children who see parents sliding into the lost land of Alzheimer's and wonder how they – both the afflicted and those who love them – will find their way out.*

We seek to conquer these and other diseases through basic biomedical research into the way genes determine our biological fate and how they can be altered to prevent or slow disease.

Our symbol is this tough and wiry tree, which embodies the survival of hope against adversity.

Douglas A. Melton

Scientist Inspired by the Child in his Life

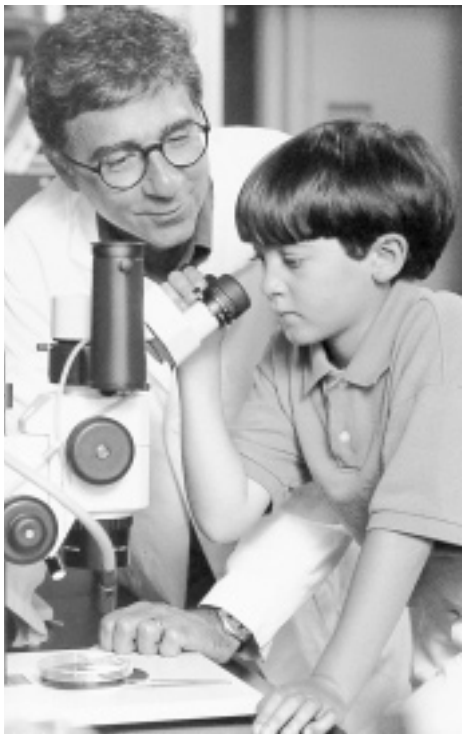
A little boy diagnosed with juvenile diabetes when he was six months old inspired Doug Melton, in a very personal way, to apply his scientific knowledge to finding the means for that little boy – and perhaps a million other people – to live normal lives.

The needs of his son Sam, now 8 years old, have turned Dr. Melton's attention in recent years from the more general questions that typically concern developmental biologists to the very specific one of how to grow a pancreas. He has become a crusader as well as scientist – leaving his Harvard lab to urge Congress to agree to federal funding of stem cell research and playing a public role to increase support for diabetes research.

In the process, he has shared his private agony with many, describing the daily regimen of injections and blood tests, diet and exercise needed for Sam to survive each day.

"Sam must face a very uncertain future," he said at a White House ceremony in June. "This is more than any child should have to think about. We can cure diabetes… I am unwilling to accept the enormity of the medical and psychological burden that diabetes imposes on children, and I am personally devoted to bringing it to an end for Sam and everyone who suffers from this awful disease."

This effort by the newest appointee to the Scientific Advisory Board of the Stowers Institute illustrates the potential that basic research represents for saving lives and improving people's health. While most research is not so obviously focused toward a cure, it opens many doors to research paths that scientists can follow to worthwhile results in curing and preventing devastating diseases, including cancer, Alzheimer's and heart disease, in addition to diabetes.



Doug and Sam Melton *(Photo courtesy of Juvenile Diabetes Foundation)*

Dr. Melton, who is chairman of the Department of Molecular and Cellular Biology at Harvard, joins three other prominent scientists on the Stowers Institute advisory body. The chairman is Dr. Leroy Hood, who is chairman of the Department of Molecular Biotechnology at the University of Washington School of Medicine. Other members are Dr. Eric Davidson, Norman Chandler Professor of Cell Biology at California Institute of Technology, and Dr. Michael Levine, Professor of Genetics and Developmental Biology at the University of California-Berkeley.

The Scientific Advisory Board created the scientific mission of the Stowers Institute, focusing on a multidisciplinary, systems approach to genomics study. The Board also directed the recent search for the first scientists to head laboratories in the Stowers Institute when it opens its doors for research toward the end of 2000.

Born in Chicago, Dr. Melton earned a bachelor's degree in honors biology from the University of Illinois, then went to Cambridge University in England as the recipient of a Marshall Scholarship. He earned a B.A. in history and philosophy of science at Cambridge, then remained there to earn a Ph.D. in molecular biology at Trinity College and MRC Laboratory of Molecular Biology.

He joined the Harvard faculty in 1981. In addition to chairing his department, he is a Howard Hughes Medical Institute investigator and principal investigator at the Juvenile Diabetes Foundation Center for Islet Cell Transplantation at Harvard Medical School. He is also co-director of the Center for Genomics and Proteomics that Harvard recently began to organize, an undertaking that shares many of the concepts that form the research mission of the Stowers Institute.

Most of Dr. Melton's early research, which won him election to the National

"I am unwilling to accept the enormity of the medical and psychological burden that diabetes imposes on children, and I am personally devoted to bringing it to an end for Sam and everyone who suffers from this awful disease."

Academy of Sciences in 1995, was aimed at understanding how genes, right after fertilization, set up the body pattern of the early embryo. In one part of that work, using frog embryos, he discovered that there is a localized information molecule in cells at the bottom of the egg that encodes a protein telling the cells what to do. In other work, he found that becoming a nerve cell is a default, or pre-disposed, state, while inductive signals are needed for a cell to become skin. By contrast, biologists had long assumed that making a nerve cell was the more complicated endeavor.

But in recent years, driven by love for his son, he has become fully focused on how the body makes an organ – in this case the pancreas. In an extremely ambitious pursuit, he is looking for a way to make pancreatic tissue in culture for transplanting into diabetics. He wants to accomplish that by starting off with stem cells, which have stirred great interest as a possible tissue repair kit for many diseases.

"The pancreas has an enormous medical significance," explained Dr. Melton. "It has a special cell called the beta cell, which makes insulin. It reads the amount of glucose, or sugar, in the blood, then secretes insulin so our bodies can use it. But in the case of diabetes the pancreas is dysfunctional."

The ability to grow pancreatic tissue, he pointed out, would have an enormous impact on reducing health care costs. The United States alone currently spends $105 billion a year treating diabetes – roughly seven times the entire budget of the National Institutes of Health, the primary underwriter of basic biomedical research. And, for unknown reasons, the problem seems to be growing. About 16 million people suffer from diabetes in this country, of which about 1 million have Type 1, or juvenile diabetes, the most severe form.

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Working Conditions Gritty

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Many of the people building the Stowers Institute, like Mr. Jarman and Rick Fortner, grew up on Missouri farms. Farm life taught them the practical skills that launched them into construction.

"My dad worked in the city," recalled Mr. Fortner. "Basically, my mom and I ran the farm. So at an early age I learned how to work and how to make things work."

Some others, like Timmie Richardson and Mr. Seiter, turned from jobs with limited futures to the greater promise offered by rigorous physical work. Still others are the second or third generation of their families in the same building trade.

Robert Parra, who directed the Havens Erectors crew that did ironwork on the administrative building, graduated from college, became a secondary special education teacher and wrestling coach. But after a few years, he decided he could provide a better life for his two gifted daughters by falling back on the ironworking trade of his father, brother and uncle.

One day, he recalls, he went to the Kansas state prison at Lansing to work on an expansion and as the construction crew was being escorted through the prison he saw a former student – now an inmate. "I said, 'Isaac, what happened?' And he said, 'Ah, Mr. Parra, I made a mistake, but it will never happen again.'"

Ed Hale, son of a pipefitter, started his apprenticeship in pipefitting as a 17-year-old – on the Monday after he graduated from William Chrisman High School in Independence, Mo., in 1962. Gary Chumley started his career in electricity the day after he graduated from Wyandotte High School in Kansas City, Kan., in 1958. Jerry Schaefer started in a summer sheet metal job 14 years ago, then grew through the trade and became an owner of the company. Jack Searcy followed his father and three uncles into sheet metal work. Timmie Richardson's son has followed her into construction labor.

"When I started in construction 30 years ago you didn't even carry a pencil; now we have computers," said Mr. Searcy, who regularly uses e-mail to keep tools and materials in the pipeline for his sheet metal crews.

Most can recall distinctive things about other construction projects on which they have worked, but they say two things make this job stand apart. First, there is the intense involvement of the Stowers family in the project. Jim and Virginia Stowers make regular Sunday visits to the site with son-in-law Jeff Johnson, project manager. And Mr. Stowers often roams the site on Friday afternoons with old friend Jack Jonathan, both of them with cameras in hand.

Beyond that, the people building the Stowers Institute express awe at the mission of the Stowers Institute – basic research to contribute to better treatment or cures for major diseases.

As Timmie Richardson explained: "I lost all my family to cancer. My aunts and uncles and father died of it – and my mother has cancer now. It means a lot to me when Jeff comes around and tells me what a particular area that we are building will be used for. I was first on this job, and when we finish I want to be the one to vacuum up the last little crumb of wood."

"Between one in 85 and one in 200 newborns will be fully insulin dependent, that is, will be a Type 1 diabetic, by the age of 18," he said. "That is close to an epidemic….It's obvious that if we understood, with these functional genomics approaches, how genes make cells and organs, that would have a long-term significance for treating disease."

Stressing the importance of basic research in providing eventual cures for diseases, he said: "It's not widely appreciated, I think, the power of developmental biology to affect the normal maintenance and repair of the adult. If you take a simple thing like the heart and did a literature search you'd find innumerable papers on the function of the heart, on the disease of the heart, on the drug effects and so forth. But very few on how to make a heart.

"It has been, to some sense, a prejudice of the medical community that if you want to fix the adult you study the adult. I think that an equally valuable approach is that if you want to understand how to regenerate adult tissue – to stop the process of aging, to cure cancer – don't concentrate only on the adult. But let's learn how the organism made those body parts in the first instance."

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