

Stowers Institute Principal Investigator Linheng Li (front right) and his research team unravel some of the mysteries of stem cell niches. Front row from left: Wenjia Wang, Jeff Haug, Teri Johnson, Xi He. Back row from left: Jason Ross, David Scoville, Jiwang Zhang, Donna di Natale, Leanne Wiedemann.

Jim and Virginia Stowers believe basic research of the highest quality will lead to practical solutions for human disease. This important research is a long-term process, and it may seem excruciatingly slow for those awaiting breakthrough treatments for presently incurable illnesses. But it will, ultimately, point the way to better means of preserving health and preventing disease. Stowers Institute scientists pursue the dream of Jim and Virginia Stowers by dedicating their professional lives to basic research. The results of their innovative research appear regularly in the world's leading scientific journals.

Inside this issue . . .

- Dr. Olivier Pourquié discovers a new and unexpected molecular mechanism to explain how vertebrae develop in embryos — one of many steps required to understand spinal cord deformities (Page 2).
- Dr. Linheng Li turns his groundbreaking analysis of stem cell niches toward an understanding of the pathogenesis of intestinal polyposis disease (Page 4).
- The Stowers Institute initiates new programs to benefit high school teachers in the Kansas City area and college students across the country (Page 6).
- National and international leaders discuss their latest research at Stowers Institute symposia, and local scientists and students present their own findings (Page 8).
- Stowers Institute investigators play prominent roles in the peer review process at the NIH and as editors of peer-reviewed scientific journals (Page 10).



A TOP TEN HIT:

Olivier Pourquié Sheds Light on Mechanisms in Vertebrae Development

In the early 19th century, natural scientists seeking to understand animal biology naturally turned to anatomy, and they observed a strikingly common feature: segmentation. Worms, insects, and mammals all have repeating body segments, a pattern that is particularly obvious in the human spine.

Vertebrae are generated early during embryogenesis, when body plans are being established. Malfunctions in this process can result in severe spine deformities.

processes that orchestrate segmentation of vertebrae in chicks and mice has stimulated increased interest in the field while bringing him many recent honors.

A Segmentation Clock for Somite Development

Vertebrate embryos develop in a head-to-tail sequence, first forming anterior structures, like the head and neck, and then progressively adding

“New somites form in a defined rhythm, implying an exquisite coordination in the complex cellular movements responsible for the embryo’s growth and patterning,” Dr. Pourquié says. He calls this underlying temporal coordination the “segmentation clock.”

Dr. Pourquié showed that the segmentation clock ticks according to varying expression of genes important in fetal development. When the genes flash on, a new, immature somite forms at the embryo’s tail end. Later, the same gene flashes again and another segment forms at the tail, elongating the head-to-tail axis.

This oscillating gene expression is the molecular mechanism of the segmentation clock (Figure 2). Each oscillation of the segmentation clock produces one somite. As the tail elongates away from a somite, that somite begins to mature and progressively takes on more features of fully formed vertebrae.

Dr. Pourquié and Postdoctoral Associate Julien Dubrulle discovered that Fibroblast Growth Factor 8 (FGF8) keeps the cells near the tail in an immature, undifferentiated state compatible with continued growth.

Over time, the concentration of the FGF8 signal dissipates and gradually disappears as the tail elongates away from the somite, keeping it at a fixed distance from the tail. The temporal pattern of the segmentation clock creates a repetitive spatial pattern and coordinates the rhythmic generation of vertebrae.



Associate Investigator Olivier Pourquié and his laboratory team take satisfaction in the accolades recently bestowed on his segmentation clock research by the American Association of Anatomists, Nature’s Milestones in Development, and the Faculty of 1000 (Page 9).

Yet as obvious — and important — as the segmentation process is, very little attention has been paid to uncovering its molecular mechanism. Dr. Pourquié, associate investigator at the Stowers Institute, is changing that. His seminal research in understanding the molecular

more posterior structures, such as the trunk and tail (Figure 1).

The posterior part of the embryo grows at the tail bud, where immature cells proliferate and generate the body axis. As it grows, the new tissue becomes segmented into somites, or longitudinal sections.

The Search for Answers

As with most important discoveries, this one raises new questions. First and foremost, how is the repetitive spatial pattern created? Dr. Pourquié thinks he has the answer.

Gene transcription produces multiple copies of messenger RNA (mRNA) that are translated into an amino acid chain comprising FGF8. Because the FGF8 gene is transcribed, or turned on, only at the tail, and not further up in the somites, you would expect to find the mRNA only at the tail. But, Dr. Pourquié found evidence of FGF8's mRNA further up the spatial gradient as well.

"We believe it is mRNA degradation that drives the establishment of the gradient," explained Dr. Pourquié. "As the mRNAs gradually degrade, the corresponding decrease in FGF8 protein concentration allows the somite to mature at a defined distance from the tail bud."

Dr. Pourquié currently is investigating what controls the number of segments in the body axis and how the number of somites that will become cervical vertebrae in the neck or thoracic vertebrae along the rib cage are determined in different organisms. Long-necked animals such as swans may offer clues into these next phases of research, so Dr. Pourquié is seeking a suitable source of fertilized eggs to incubate, which would allow him to study embryogenesis in swans.

"This is an area of research that I find intriguing," says Dr. Pourquié. "I am looking forward to continuing the search for new answers to questions, and new questions to answer." 🌱

Figure 1: Vertebrae derive from embryonic somites. This sequence illustrates the head-to-tail vertebral development of a chicken. The two-day-old embryo (left) has 11 somites. The black lines indicate the position of those somites on the ten-day old embryo (right) with a fully developed skeleton. The five most anterior somites are incorporated into the skull (not shown on the right panel).

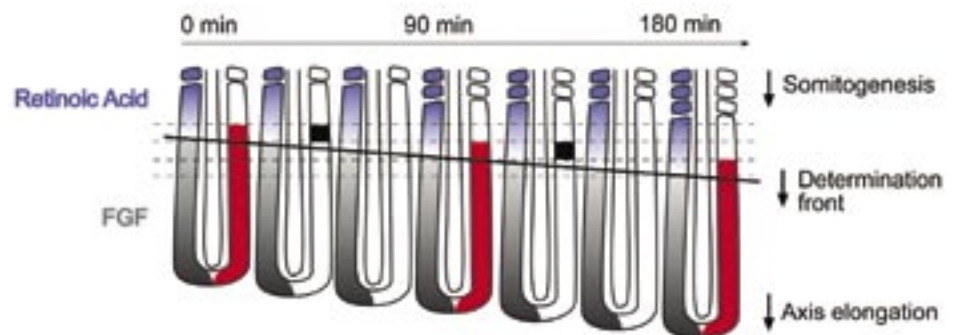


Figure 2: The clock and the determination front model for somitogenesis. The determination front marks the level at which cells respond to the segmentation clock. It is defined by gradients of two signaling molecules (blue and red) that are mutually antagonistic: as one increases, the other decreases. As periodic signals from the segmentation clock reach the cells at the front, they begin to express specific genes (black) that enable the cells to differentiate. This mechanism translates the temporal periodicity of the clock into the spatial periodicity of the segments during extension of the body axis (anterior section is at the top).

Recent Papers

Pourquié, O. (2003) The segmentation clock: converting embryonic time into spatial pattern. *Science*, 301:328-330.

Dubrulle, J., Pourquié, O. (2004) FGF8 mRNA decay establishes a gradient that couples axial elongation to patterning in the vertebrate embryo. *Nature*, 427:419-422.

LINHENG LI:

The Stop and Go Signals in Stem Cell Niches

Umbilical cord blood contains blood stem cells that, in the event of a serious disease, can sometimes be used to replenish the entire blood system without the need of a difficult bone marrow transplant. This prospect offers comfort to some new parents who choose to save umbilical cord blood to protect their children against future health risks. But even this novel procedure is no guarantee.

“Unfortunately, only about five to 10 milliliters of cord blood can be saved, and that quantity does not really contain a great many stem cells,” explains Stowers Institute Assistant Investigator Linheng Li. “Furthermore, scientists still have difficulty getting stem cells to multiply into the quantities such therapies might require.”

Dr. Li is examining alternative solutions to this and other problems of human health in his laboratory. His research focuses on the physical surrounding, or niche, that houses stem cells in the body and helps regulate their growth.

Dr. Li is especially interested in what happens to stem cells when they are removed from their niche. Outside of their niche, these cells no longer proliferate readily, and this can cause problems for therapeutic bone marrow transplantation. Additionally, he is interested in understanding how abnormal signaling in the intestinal stem cell niche can cause too much stem cell growth and lead to polyposis disease and colon cancer — a leading cause of death in the western world.

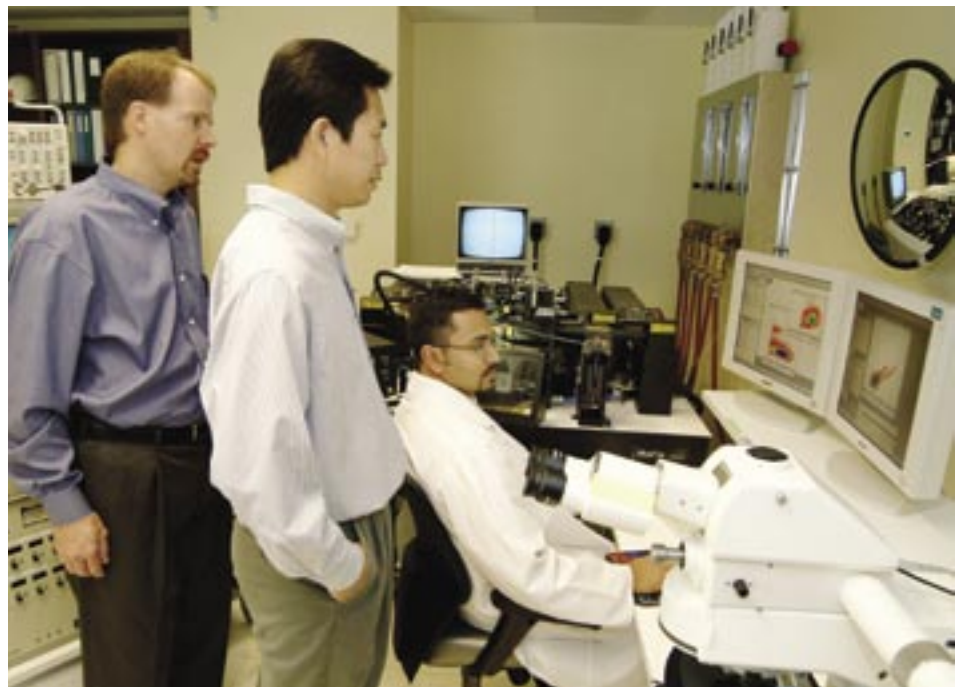
The Nurturing Niche

With collaborators at the Stowers Institute and other institutions, Dr. Li found the elusive niche for blood stem cells in 2003* (*2003 Annual Report*). His findings resolved a quarter-century search by demonstrating how certain osteoblast cells in the bone’s interior lining form miniature caves where the marrow’s stem cells nestle. They also demonstrated that expanding the population of osteoblast niche cells caused a parallel increase in hematopoietic stem cells in the bone marrow.

Dr. Li’s lab is now working on reconstituting the niche in the laboratory to create an incubator for expanding the stem cell population.

“We want to get quantities suitable for treatment in a clinical setting to determine if this work can be translated into therapy for human blood diseases,” he says. Recently, they observed that isolated osteoblast cells form a niche-like structure in a tissue culture dish (Figure 1).

“However, the primary osteoblasts tend to either differentiate or undergo apoptosis and die after a short time in culture,” he says. “Now we’re focusing on isolating osteoblastic niche cells using flow cytometry and further establishing them as cell lines. This would allow us to investigate the molecular mechanism and genetic pathways that regulate stem cell development and self-renewal in the bone marrow.”



Linheng Li; Jeff Haug, managing director of the Cytometry Facility; and Sach Jayasinghe, cytometry research technician II, work together in the Cytometry Facility.

Ultimate Goal: Regenerating Intestines

In defining the bone marrow stem cell niche, the Li lab identified a signaling gene, bone morphogenetic protein (BMP), that inhibits stem cell proliferation. They determined that silencing the BMP signal at the niche increased the stem cell population, and it seems that this holds true for other niches as well.

“It now appears that BMP’s regulation of the stem cell number is not limited to the hematopoietic system, but also is seen in the intestinal system,” Dr. Li says.

In a variety of intestinal diseases, abnormal growths called polyps form on the mucous lining and cause obstruction — a process partially attributed to runaway activity of stem cell populations. To investigate the underlying molecular mechanism, the lab analyzed intestinal stem cells in mutant mice lacking the BMP signal.

“The intestines exercise a controlled balance between the genetic pathways that stimulate stem cell proliferation and those that inhibit it,” Dr. Li explains. “This balance ensures that the niche produces neither too many nor too few stem cells.”

Significantly, three diseases — juvenile polyposis syndrome (JPS), juvenile intestinal polyposis, and Cowden’s disease — have been linked to mutations in signaling genes (BMPRI1A, SMAD4, and PTEN, respectively).

Since BMP and PTEN (a tumor suppressor) normally inhibit intestinal stem cell division, Dr. Li hypothesized that these genes malfunction in a way that

encourages too much cell growth in the intestinal lining. To explore an individual gene’s role in a complex system, scientists often “knock out” or disable the gene and observe the effect in a model organism. To that end, Dr. Li’s lab performed genetic manipulation to block BMP signaling in mice. As expected, the mutant mice developed intestinal polyposis, mimicking human juvenile polyposis.

Dr. Li’s results, reported in the October issue of *Nature Genetics***, found that BMP’s signal specifically inhibits signaling of the Wnt gene. The Wnt pathway promotes intestinal self-renewal by sending an adhesive-like protein, b-catenin, into the stem cell nucleus, triggering stem cell division. Essentially, the Wnt “go” signal competes with the BMP’s “stop” signal, while PTEN mediates their struggle like a police officer making sure traffic runs smoothly. When the BMP function is lost, Wnt increases and escapes PTEN’s regulation.

“We detected duplicated stem cells in the polyp region,” Dr. Li observes. This indicates that the unchecked Wnt signal increases self-renewal of stem cells. Presumably, the overproduction of stem cells sets off a frenzy of cell division that leads to the growth of a polyp.

“In this work we have identified biological markers to recognize intestinal stem cells,” says Dr. Li. “We showed the signaling components of the BMP, PTEN, and Wnt pathways at the level of single stem cells in a complicated mammalian system.”

Dr. Li recently was awarded the second annual Hudson Prize (page 9) and plans to use the grant money to isolate and

further study the intestinal stem cells.

“With this award, we can undertake additional experiments that might lead to something very important,” he says. “The ultimate goal of studying and characterizing the intestinal stem cells is to be able to regenerate the intestine and to develop potential treatments for colon cancer, ulcers, or other intestinal diseases.”



Figure 1: Image of osteoblast niche for hematopoietic stem cells forming in lab culture. Certain osteoblasts elongate, forming a smooth arch on one edge and a jagged shape, like a bone cavity, on the other edge. The stem cells nestle in the arch.

Recent Papers

* Zhang, J. , Niu, C. , Ye, L. , Huang, H. , He, X. , Tong, W. G. , Ross, J. , Haug, J. , Johnson, T. , Feng, J. Q. , Harris, S. , Wiedemann, L. M. , Mishina, Y. and Li, L. (2003). “Identification of the haematopoietic stem cell niche and control of the niche size.” *Nature*, 425(6960): 836-41.

** He, X. C. , Zhang, J. , Tong, W. G. , Tawfik, O. , Ross, J. , Scoville, D. H. , Tian, Q. , Zeng, X. , He, X. , Wiedemann, L. M. , Mishina, Y. and Li, L. (2004) BMP signaling inhibits intestinal stem cell self-renewal through suppression of Wnt-beta-catenin signaling. *Nature Genetics*, 36, 1117-1121. Commentary 1038-39.

Reaching Out to the Region

Science Teachers Access to Research at Stowers (STARS)

When Abby Freeman arrived at the Stowers Institute in November 2003 as vice president for administration, she began working on a way for Kansas City teachers to benefit from the Institute's extraordinary research. Ms. Freeman had participated in a similar program at the University of Texas Southwestern Medical Center in Dallas, so she understands that developing future researchers depends on good high school science teachers getting their students excited about science. That is why Ms. Freeman coordinated the launch of the STARS program this November.

"We did not want to duplicate what already existed here," she says of programs sponsored by the Kansas City Star and by Science City at Union Station that target all students and provide supplemental materials and classroom kits for any interested teacher. "We wanted to add a missing layer of outreach to the area schools while remaining within Stowers' capabilities and purposes. As a research institution, we cannot provide hands-on lessons, but we can share access to the exciting new discoveries in biomedical research that secondary science teachers may not otherwise have.

"When the participating teachers become excited and invigorated about science, they can encourage students to study science in college," she says. "We believe programs like STARS can ultimately increase the number of science students in colleges and universities."

Stowers Scholars Program

For college students who are studying science, Ms. Freeman administers a summer internship program. The Stowers Scholars Program encourages students to consider graduate studies in basic research and careers as research scientists.

"Impressionable college sophomores and juniors see what it is like to do basic research under the mentorship of a principal investigator in a top-notch lab where people love what they do," explains Ms. Freeman. In 2004, 80 students applied and 8 were accepted to an intensive 8-week experience in a research lab.



Abby Freeman works with Stowers Scholars. Applications for the 2005 Stowers Scholars Program are due by Feb. 4, 2005. For more information visit Training Programs at www.stowers-institute.org.

Stowers Scholars 2004 Projects

Student Scholar	School and Project
Brian Chase <i>Ting Xie Lab</i>	Massachusetts Institute of Technology "Identification of Genes for Germline Stem Cell Self-Renewal in the <i>Drosophila</i> Ovary by Overexpression Screens"
Laura Hughes <i>Chunying Du Lab</i>	Northwestern University "Identification of Caspase-2 Substrates"
Jessica Leonardi <i>Peter Baumann Lab</i>	Texas A&M University "Mapping the Essential Domain of Pot1"
Kathleen Lindstrom <i>Scott Hawley Lab</i>	University of Kansas "A Germline Clone Screen to Identify Genes Involved in Meiosis"
Erin Miller <i>Jennifer Gerton Lab</i>	Kansas State University "Deletion Mutagenesis of Budding Yeast MND1"
Alyse Prince <i>Susan Abmayr Lab</i>	Carnegie Mellon University "Analysis of Defects in Muscle Development Through the Generation of Mutations in the <i>sns</i> and <i>Blow</i> Genes"
Lauren Sisel <i>Paul Kulesa Lab</i>	University of Missouri-Rolla "Multicolor Labeling and Time-lapse Imaging of Neuronal Precursor Cells in Living Chick Embryos"
Erin Smith <i>Jerry Workman Lab</i>	Truman State University "Cloning and Expression of Novel <i>dAda1</i> Protein"

BioMed Valley

The arduous process of advancing discoveries out of basic research labs into the hands of physicians who treat patients can take a decade or more. Even before the Stowers Institute opened its research facility in Kansas City, Jim and Virginia Stowers wanted to do everything possible to ensure that research conducted here would benefit people as quickly as possible. They also wanted to see the Institute boost the economy of the Kansas City area — a geographic region that Jim and Virginia call BioMed Valley. Now, they have announced an innovative way to fulfill both goals through the creation of the BioMed Valley Partnership.

This non-profit organization, incorporated as BioMed Valley Corporation (BVC), will directly support researchers at the University of Missouri-Kansas City, the University of Kansas, and the Stowers Institute. BVC's wholly-owned subsidiary, BioMed Valley Discoveries (BVD), will assist these three partner institutions with technology development and commercialization. The proceeds will be shared equally with the inventors and their institutions. Scientists will be directly compensated for their work, and the profits garnered by the institutions will reside in an endowment at BVC to

yield a growing stream of income in support of more basic research.

"I am unaware of any other such model," says Richard W. Brown, co-chair of the board of the Stowers Institute as well as chair of the boards of both BVC and BVD. "We want to elevate the quality of research in the region, and that will, in turn, attract more high-quality scientists and students to the partnership institutions."

"Virginia and I have been gratified to witness the efforts of our government leaders in Kansas and Missouri to support growth of excellent life science at both state universities," says James E. Stowers Jr., co-founder of the Stowers Institute. "If we all pull together to achieve the BioMed Valley dream, Kansas City can become the best place anywhere for life science research and for turning discoveries from that research into products that can help people everywhere."

A Second Home for Research

With the growing vision of BioMed Valley comes an imminent need for more research space. Bill Neaves, president and CEO of the Stowers Institute, explains that at the rate the Institute is attracting investigators, a second facility of equal size to the first will be required by the end of the decade. In preparation, Mr. and Mrs. Stowers announced earlier this year that they were committed to the expansion and were appointing an architect to integrate the new facility with the original. At the top of the scientists' request list for the expansion: creative design of common spaces to promote the social interactions that can lead to new ideas and collaborations — a hallmark of the current facility. 🌿



(From left to right) Bill Neaves, Dick Brown, Virginia Stowers, Jim Stowers, and David Welte work together to help BioMed Valley achieve its full potential.



Mike Washburn, director of Proteomics, and Paul Kulesa, director of the Imaging Center, discuss their work in their shared library area.



Ting Xie, Susan Abmayr, Chunying Du, and Arcady Mushegian meet in the cafeteria to discuss a current research challenge.

GOING TO KANSAS CITY:

Conferences at the Stowers Institute



Scott Hawley, Jennifer Gerton, and Peter Baumann worked together to coordinate the “Structural Biology of Chromosomes” conference.

Together with Assistant Investigators Jennifer Gerton and Peter Baumann, Investigator Scott Hawley organized the conference “Structural Biology of Chromosomes” on April 22 and 23. The sessions presented exciting insights into how changes in the structure of chromosomes support their proper function throughout the life of the organism.

The conference offered an innovative twist on traditional scientific networking. Each of the seven invited speakers brought along a graduate student and a postdoctoral fellow to meet with their counterparts at the Stowers Institute in small workshops.

“They had the opportunity to form links between labs with researchers at levels similar to their own, who do the work at the bench on a daily basis,” explains Dr. Hawley. “We’ve had great feedback that tells us this was a wonderful investment of effort.”

From April 30 – May 2, Associate Investigator Olivier Pourquié and Dave Burt of the Roslin Institute co-chaired a conference entitled “The Chicken

Genome: New Tools and Concepts.” At a previous workshop in Cambridge (UK) in early 2003, Drs. Pourquié and Burt established the International Chicken Genome Consortium, the first coordinated effort directed at sequencing an avian genome.

Presenters discussed the status of the chicken genome project, its place in the broader context of genome evolution, and newly developed research tools. Participants learned that the relatively small chicken genome has many fewer repeat sequences than the human genome and has undergone less “shuffling” than rodents and fish, suggesting that it may be closer to ancestral vertebrate chromosomes.

“The meeting helped shape the realization that the chick will be a powerful experimental model species for researchers working with other systems,” says Scientific Director Robb Krumlauf.

“The Chicken Genome: New Tools and Concepts” was reviewed in several journals, including *Developmental Cell* and *Developmental Dynamics*.

On June 5-8, Assistant Investigator

Paul Trainor organized the 44th Annual Midwest Regional Developmental Biology Meeting and Singer Symposium with co-chairs Drs. Krumlauf and Pourquié. This was the second year that the Stowers Institute hosted the meeting. A distinguished roster of speakers discussed the latest research on spinal cord development, stem cells, embryonic development, and congenital abnormalities. The meeting provided young postdoctoral fellows and graduate student researchers with a forum for presenting and discussing their own work and mingling with national and international research leaders.

Dr. Trainor also co-chaired a symposium on stem cell science with Ken Peterson of the University of Kansas Medical Center on September 27. Plenary speakers were Mario Capecchi of the University of Utah, who pioneered many of the techniques used in stem cell research, and David Scadden of Harvard Medical School, who helped define the location of hematopoietic stem cells in the bone marrow.

“This symposium served as a catalyst for the scientific community in Kansas and Missouri to meet regularly to exchange ideas and techniques advancing the understanding of stem cell science and its possible applications,” says Dr. Trainor.



Paul Trainor organized the 44th Annual Midwest Regional Developmental Biology Meeting and Singer Symposium, which was co-chaired by two Stowers Institute colleagues.

Awards and Distinctions

Associate Investigator **Olivier Pourquié's** paper in the January 29, 2004 issue of *Nature* attracted attention as a landmark contribution towards understanding vertebrate development. The editors called his findings on the role of mRNA decay in the segmentation process (pages 2-3) "an entirely new and unexpected mechanism for forming morphogenetic gradients." The *Faculty of 1000*, an organization that screens the thousands of weekly journal articles to highlight the few most important, ranked Dr. Pourquié's article at the top of the ten most significant recently published papers in all biology by early March. Meanwhile, *Nature* credited the most recent of their 24 "Milestones in Development" (right) to Dr. Pourquié's discovery of the segmentation clock. He was also awarded the 2004 Harland Winfield Mossman Award in Developmental Biology from the American Association of Anatomists (AAA). Dr. Pourquié holds a NIH R01 grant and serves on a NIH Study Section (Page 10).

Assistant Investigator **Linheng Li** received the 2004 Hudson Prize for his discovery of the hematopoietic stem cell niche. M.R. Hudson, the founder of Hudson Oil Co. and later Fisca Oil Co., established the Texas-based Hudson Foundation in 1991 to further his lifelong interest in supporting education, medical research, children's issues, and the arts. The foundation established programs at the University of Texas Southwestern Medical Center in Dallas and the Stowers Institute to recognize outstanding young scientists who have made important discoveries. Associate Investigator **Ting Xie** received the inaugural prize in 2003 for defining the stem cell niche in *Drosophila* ovaries.

"The \$50,000 stipend will enable Dr. Li to pursue his exciting work on stem cells more aggressively," says Bill Neaves, president and CEO of the Stowers Institute.

Assistant Investigator **Paul Trainor** received a five-year grant from the National Institutes of Health (NIH) to study how neural crest cells contribute to the formation of the head and face during mammalian embryonic development. Head and facial abnormalities constitute one of the largest groups of congenital birth defects. One focus of Dr. Trainor's lab is Treacher Collins syndrome, which develops very early during pregnancy and encompasses cleft palate, problems with jaw formation, and ear and hearing defects.

Investigator **Ron Conaway's** NIH MERIT grant was renewed for another five years. This category of grant is reserved for investigators who are highly productive and well established leaders in their field of study. Dr. Conaway investigates the role of RNA polymerase in gene transcription.

Two *Nature* Milestone Researchers Now at Stowers

Nature's Milestones in Development series highlights significant research discoveries in developmental biology over the past 100 years. A group of 34 developmental biologists helped select 24 milestone achievements that revealed fundamental developmental mechanisms conserved across the animal kingdom. The most recent addition to the series, Milestone 24, highlights **Dr. Pourquié's** work on somitogenesis and molecular clocks completed at the Developmental Biology Institute of Marseille, France. An earlier Milestone, no. 11, credits the contribution of **Dr. Rob Krumlauf**, scientific director, when he worked at the National Institute for Medical Research in England, where he discovered that mouse and fly *Hox* genes have similar spatial and functional organization.



Milestone #11: Homeotic Genes and Colinearity
<http://www.nature.com/milestones/development/milestones/full/milestone11.html>

Milestone #24: Somitogenesis and Molecular Clock
<http://www.nature.com/milestones/development/milestones/full/milestone24.html>

Extracurricular Activities

Investigators at the Stowers Institute for Medical Research do not spend all of their time in their labs and classrooms. Many also contribute time to reviewing the work of their colleagues on behalf of the National Institutes of Health (NIH) and various scientific journals.

“You learn in science that there are lots of service roles,” explains Scientific Director Robb Krumlauf, “whether it’s hosting a meeting to educate scientists, reviewing journal articles, or participating in the grant review process.”

Judging Grants

The NIH funds the largest portion of research in the United States. To ensure that these grants promote the best and most beneficial research, the NIH convenes Study Sections for each field of research and charges them with reviewing and evaluating the merits of grant proposals in that field.

“Study Sections are the heart of the peer-review process. They sustain the commitment of the NIH to fund only meritorious research,” explains President and CEO Bill Neaves. “I’m proud of the Institute’s high level of participation in the NIH peer-review process.”

Dr. Krumlauf serves as a member and co-chair of one of the two Study Sections devoted to developmental biology (Dev2), while Associate Investigator Olivier Pourquié is a member of the other major study section reviewing grants in developmental biology (Dev1). Investigator Ron Conaway belongs to a Study Section dealing with molecular biology.

“It’s important for the Stowers Institute to participate, but it is an onerous effort, requiring one full week of concen-



Robb Krumlauf, Jerry Workman, Ron Conaway, and Olivier Pourquié each serve as reviewers of requests for funding from the NIH and other organizations.

trated effort to review the grant proposals before attending a two-day meeting at NIH headquarters in Bethesda, Maryland,” says Dr. Krumlauf.

Each of the 16 or so members of a Study Section is responsible for presenting detailed reviews of approximately 10 grant proposals at each of three meetings during the year. All members listen to these reviews and then vote priority scores that determine which grants get funded.

“This participation benefits investigators at the Stowers Institute,” Dr. Neaves adds, “because Study Section members can provide insightful guidance to their colleagues about the evaluation process and how to structure grant proposals to meet the strict review standards of the NIH.”

Recently, Investigator Jerry Workman accepted an appointment to the National Cancer Institute’s Board of Scientific

Reviewers. This board evaluates research done in the laboratories supported by the National Cancer Institute and recommends funding levels for those labs.

Reviewing Papers

Another integral part of the peer-review process entails rigorous evaluation of scientific papers for publication in journals. Every Stowers investigator has been on the “reviewed” end, but several also have prominent roles on the editorial boards of leading journals.

Drs. Krumlauf and Pourquié both serve as editors of *Developmental Biology*, and Drs. Ron Conaway and Joan Conaway belong to the editorial board of the *Journal of Biological Chemistry*. Dr. Workman is a member of the Board of Reviewing Editors of the journal *Science* and is an editor for *Molecular and Cellular Biology*.

In their roles as editors, the Stowers investigators receive manuscripts for their respective journals, assign reviewers, and evaluate the critical reports to reach a final decision on acceptability for publication.

“*Science* receives ten times more papers to review than they can publish,” Dr. Workman explains. “The editors are not professional research scientists, so they assemble a board of reviewing editors who are experts in their research fields. We receive PDF files of submitted papers and must review them within 48 hours. We read to see if a paper looks like a solid piece of research that will have high impact, and we write a review paragraph that ranks it and recommends whether it should be reviewed in depth.”

Another duty for Dr. Workman is to recruit important papers to *Science* rather than competing journals. “I keep my eyes open at meetings for something interesting that is still unpublished and recommend that the investigators consider publishing it in *Science*,” he explains.

Dr. Workman says that while *Science* is looking for something “hot and sexy,” *Molecular and Cellular Biology* is more of a “workhorse” journal where a larger portion of scientific material is published. As an editor, he decides if a paper is worthy of review. If so, he sends the paper to three reviewers who may provide a list of problems for the researchers to resolve.

“It’s a good process because the additional experiments improve the quality of the published data,” he says. “This is especially good for junior scientists. And sometimes additional experiments completely change the interpretations of results.”



Joan and Ron Conaway are members of the editorial board of the *Journal of Biological Chemistry*.



Jerry Workman dedicates time to his duties as a member of the Board of Reviewing Editors for the journal *Science* and as an editor for *Molecular and Cellular Biology*.

Hope Shares®

Between January 1 and October 7, 2004, contributions of at least \$1,000, the minimum for establishing a Hope Shares® account in the endowment of the Stowers Institute, were received from, or in memory of, the following:

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Every attempt has been made to ensure the accuracy of the above list. In case of error or omission, the Stowers Institute wishes to be advised.

*Multi-year commitment

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