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Gruber installed as director of USC Norris Cancer Center

By Ina Fried

Efforts to diagnose and treat a 67-year-old man with gastrointestinal bleeding following a cardiac catheterization led to important considerations about the role of genomics in cancer research and targeted care. Stephen B. Gruber described the case during his inaugural lecture as holder of the H. Leslie Hoffman and Elaine S. Hoffman Chair in Cancer Research.

At a ceremony held April 11 in the Harlyne J. Norris Cancer Research Tower, Gruber was installed as the fifth director and the first clinician-scientist to lead the USC Norris Comprehensive Cancer Center.

Keck School of Medicine of USC Dean Carmen A. Puliafito said, "Great medical institutions require great physician leaders, and USC Norris will be even greater under Steve Gruber."

Gruber called the occasion "an extraordinary day for me." He said, "The opportunity to lead a comprehensive cancer center is truly something that I treasure." He expressed gratitude for the support of the Hoffman Chair, which allows him the freedom to innovate in his own research and to concentrate on nurturing and improving the infrastructure and support for other members of the cancer center.

Discussing "precision cancer care" and the future of genomic oncology, Gruber noted the frequent occurrence of cancer in the family of the 67-year-old patient, in spite of the fact that the man did not have any of the genetic mutations known at that time to be related to colon cancer. Sequencing the entire genome of the patient and his son—the first such sequencing at the University of Michigan—revealed eight previously unknown and potentially relevant mutations.

The case also illustrated the importance of a Sequencing Tumor Board that Gruber had set up at the University of Michigan—made up of a health behaviorist, ethicist, psychiatrist, genetic counselor, molecular geneticist, clinical oncologist and pathologist. The board established a protocol to help in determining such matters as the clinical relevance of the genomic information and how to share information with patients in a meaningful and responsible way.

Gruber is "obviously a very special guy, and it's been a real privilege to play some role in his career development," said David Ginsburg, the keynote guest speaker at the installation. Ginsburg, who was an important mentor to Gruber, is the James V. Neel Distinguished University Professor of Internal Medicine and Human Genetics at the University of Michigan Medical School.

"What's happening in genetics is nothing short of astounding," Ginsburg said. Harnessing the power of modern genetic information to improve diagnosis has already made spectacular progress, he said, but customizing treatments is still in the early stages and will take much more work.

"The future will be different," he said. "I predict that everyone will get a full genome sequencing at birth. There's a lot we have to learn, but it's an incredibly exciting time."

Brian Morri

Keck School of Medicine of USC Dean Carmen A. Puliafito (left) and David Ginsburg, the James V. Neel Distinguished University Professor of Internal Medicine and Human Genetics at the University of Michigan Medical School (right) congratulate Stephen B. Gruber at his installation as the fifth director and the first clinician-scientist to lead the USC Norris Comprehensive Cancer Center.

Nobel Laureate Roger Kornberg elucidates mechanism of transcription

By Amy E. Hamaker

The use of genetics in medicine and science is growing exponentially. Although much is known about genetic instructions being transmitted through DNA and RNA, the mechanics of how this happens haven't always been clear.

Nobel Prize winner Roger Kornberg of the Stanford University School of Medicine explained some of those mechanics, speaking to a full room on April 10 at the Keck School of Medicine of USC. Kornberg received the Nobel Prize in Chemistry in 2006 for his work on understanding how DNA is converted into RNA, a process known as transcription.

Kornberg's lecture covered highlights of his course of work on transcription over the years, as well as some of the most recent and some unpublished work. Much of his lecture focused on the enzyme RNA polymerase II found in cells with membranes. RNA Polymerase II is a complex multisubunit protein. The enzyme uses contacts within specific protein components to pull the two halves of the DNA helix apart and allows complementary RNA to form. The new RNA then separates from the DNA and exits the structure. When this structure works perfectly, the result is a faithful copy of the genetic material.

"Polymerase II is the platform on which all the other components rest in this process," said Kornberg. "If you want to understand such a complex process, you must study the structure of the components. The DNA enters the atomic resolution crystal structure as a double helix, makes a sharp bend in the middle of the structure, RNA transcription occurs and the RNA exits almost at a right angle to the DNA coming in."

Kornberg and his colleagues answered many questions about the basic functions of this system, including how a very stable DNA/complementary RNA structure can be interrupted and the RNA peeled off. He explained that protein loops called rudders and lids enforce the separation, while a fork loop prevents the unraveling from continuing on to the active center, where the RNA is being produced, and stopping the whole process.

During the mid 1980s, another component that is absolutely required in RNA transcription

See **KORNBERG**, page 3

Steve Cohn

The new multi-disciplinary office, expected to open its doors to patients at the end of the month, will house more than 40 faculty physicians.

Keck Medical Center opens Pasadena office

By Tania Chatila

USC's academic medical center is expanding its reach into the San Gabriel Valley with its largest satellite office yet.

The Keck Medical Center of USC Pasadena made its debut at a special ribbon-cutting ceremony and open house on April 10, attended by nearly 150 USC staff, physicians and members of the local community.

The multidisciplinary office—which is expected to open its doors to patients at the end of the month—will house more than 40 faculty physicians representing more than 15 specialties including oncology, ophthalmology, urology, gynecology, surgery and cardiovascular services.

"When USC purchased our two hospitals three years ago, it was always our hope to be able to provide world-class medical care in the communities where our patients live and work," said Scott Evans, chief operating officer and interim chief executive officer of Keck Hospital of USC and USC Norris Cancer Hospital. "This office will cater to a large patient base in Pasadena and the surrounding communities, making it more convenient for them to access the quality, compassionate care they have come to know is a hallmark of the Keck Medical Center of USC."

At 22,000 square feet, the ambulatory care center is the medical center's largest specialty physician office outside of the Health Sciences campus. The suite occupies the entire fourth floor of the Huntington Pavillion, at 625 S. Fair Oaks Ave., Suite 400, and will consolidate what were several scattered medical practices into one location. The office, which

See **PASADENA**, page 3

Acid reflux device gives two patients new hope for normal life

‘I had GERD for the last 30 years, so I’ve kind of forgotten what it’s like to live without it. Now, [after surgery] I have no reflux whatsoever. I hate to use the word, but it’s a miracle at this point.’

—Rodd Foster, patient at the Keck Medical Center of USC

By Alison Trinidad

One man looks forward to being able to sit down and have dinner with his family, while another dreams of playing music again. Years after struggling from the pain, discomfort and embarrassment of severe acid reflux, both are pinning their hopes for a normal life on a seemingly simple device and 20-minute surgical procedure.

Gastroesophageal reflux disease (GERD) inflicts misery on nearly 20 percent of the U.S. population. Most people have experienced the occasional discomfort of what is commonly known as heartburn, but millions live with it daily, suffering damage to the esophagus that in some cases leads to cancer.

On April 9, Rodd Foster, 60, and James “Shane” Barmby, 58, patients at the Keck Medical Center of USC, were among the first in the nation to have the LINX Reflux Management System implanted since the Food and Drug Administration approved its use on March 22. The device, a bracelet of magnetic, titanium beads that goes around the lower end of the esophagus, was tested in clinical trials at the Keck Medical Center of USC, which is one of only three centers in California authorized to use it.

“I had GERD for the last 30 years, so I’ve kind of forgotten what it’s like to live without it,” said Foster, a plumbing contractor from Canyon Country who could not sit down to eat dinner with his family after 3 p.m. “Now, [after surgery] I have no reflux whatsoever. I hate to use the word, but it’s a miracle at this point.”

John Lipham, associate professor of surgery at the Keck School of Medicine of USC, led the clinical investigation of the device as part of his ongoing work to find alternative ways to treat GERD.

Jon Nalick

Rodd Foster, patient at the Keck Medical Center of USC, gives a pre-operation interview about the challenges he has faced resulting from gastroesophageal reflux disease. Within days of his operation Foster said his decades-long symptoms had vanished.

“This device is a huge advance for the treatment of reflux, which affects millions of people in the U.S.,” Lipham said. “It addresses a gap in treatment of patients who suffer from GERD but no longer respond well to medication therapy.”

Implantation of the LINX system, manufactured by Minnesota-based Torax Medical Inc., is a procedure that can be completed in 15 to 20 minutes, Lipham said.

In addition to USC, Stanford and the University of California, San Diego, are also approved to implant the device.

“The Keck Medical Center of USC delivers world-class medicine to its patients every day thanks to innovative research by doctors like John Lipham,” said Scott Evans, COO and interim CEO of Keck Hospital of USC.

Lipham, who has worked with the device since its inception, says the LINX system is best for patients with mild to moderate reflux that cannot be adequately controlled by medication or for patients who do not want to take medication to manage the disease. Both Foster and Barmby, who were taking a cocktail of antacids to little avail, were good candidates for the procedure.

“When Dr. Lipham told me I had acid reflux and was the perfect candidate for this device, I started crying,” said Barmby, an actor and country musician who had been sick for years but continuously misdiagnosed. “For the last three years, I haven’t played the guitar. If Dr. Lipham can fix me, I’ll be able to play again.”

Traditionally, reflux disease is treated using a surgical procedure called a Nissen fundoplication, which involves recreating the esophageal sphincter. While fundoplication is recommended for those with severe reflux, it is a complicated procedure that prevents the ability to belch or vomit and often leads to bloating or gas problems.

The new LINX device, which has been available in Europe for about two years, is designed to augment the patient’s native esophageal sphincter and return it to a competent valve. The magnetic beads open with pressure, allowing patients to belch, vomit and swallow normally. By allowing patients to belch normally, the device allows air to escape from the stomach, preventing the gas and bloating issues.

Lipham said his patients have had no major complications with the device, though some in the clinical trial have reported difficulty swallowing that dissipates after the first month. The most common adverse events experienced with the LINX included difficulty swallowing, pain when swallowing food and chest pain.

It is important to note that patients with LINX will no longer be able to undergo magnetic resonance imaging (MRI) procedures. The magnetic beads interfere with the machine and can cause the device to be damaged.

Video of Lipham and his patients is online at: http://tinyurl.com/85f8uae.

Keck Hospital employees ratify new three-year contract that boosts pay

Five hundred and seventy-two employees at Keck Hospital of USC have voted to ratify a contract between USC and the National Union of Healthcare Workers (NUHW). The three-year contract is effective through April 30, 2015.

Hospital leadership commended the negotiating teams on both sides for successfully reaching consensus on a contract that meets the needs of employees and the organization. The total number of employees at Keck Hospital is 2,584.

“Our goal throughout the negotiations has been to develop a contract that reflects the commitment by all sides to provide exceptional care for our patients and ensure the success of Keck Hospital,” said Scott Evans, interim CEO and COO of Keck Hospital of USC. “This contract underscores the pride we all have in our academic medical center and the dedication to our patients, research and education.”

Contract highlights include:

- Salary increase over four years to maintain competitive compensation for staff
- Increase in paid time off
- Increase in tuition reimbursement
- Increase in USC contribution to retirement plan

Keck Hospital of USC and USC Norris Cancer Hospital are part of the Keck Medical Center of USC, which also includes the more than 500 faculty physicians in the Keck School of Medicine of USC. Keck Medical Center of USC was launched in 2011 thanks to a transformative $150 million gift from the W. M. Keck Foundation.

Save the Date

The USC Norris Cancer Hospital’s Image Enhancement Center will host an open house from 10 a.m. to 2 p.m. on April 26, offering visitors an opportunity to see the specialized services it can offer to patients.

The center, in Room 1362 on the first floor of the USC Norris Cancer Hospital, helps patients undergoing chemotherapy and/or radiation cope with any alterations in their appearance that may result from the treatment, including hair loss and changes in complexion.

The Weekly

Next Issue: April 27

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Steve Cohn

From left, USC dignitaries Char Ryan, Edward Crandall, Tom Jackiewicz, Scott Evans and Vaugn Starnes join Pasadena Mayor Bill Bogaard at the April 10 ribbon cutting. The event attracted nearly 150 USC staff, physicians and members of the local community.

PASADENA: Keck Medical Center expands its reach

Continued from Page 1

can accommodate up to 400 patients a day, also includes an onsite infusion center with a laboratory and pharmacy.

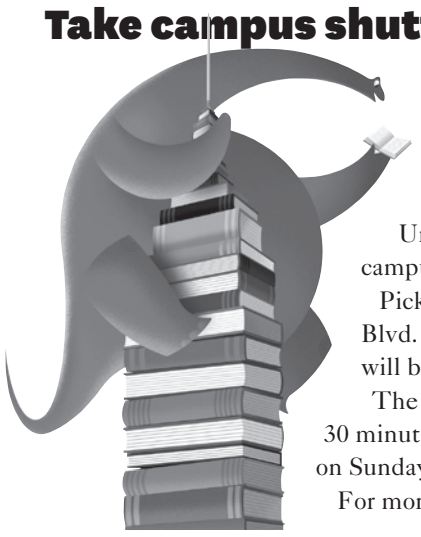
"The Keck Medical Center of USC Pasadena adds to our city's growing reputation as a premier destination for medical services and biomedical research," said Bill Bogaard, mayor of the City of Pasadena. "Our citizens have relied on the expertise of USC faculty physicians for years. We appreciate this important expansion of USC's world-class services."

This is the fourth satellite office for the Keck Medical Center of USC, with other locations in downtown Los Angeles, Beverly Hills and La Cañada Flintridge.

Tom Jackiewicz, senior vice president and CEO for USC Health, said these off-site physician practices are part of a larger plan to expand USC's network of care.

"We are leveraging every opportunity we have to bring our brand of medicine to patients throughout the region, whether that be through clinical partnerships or satellites facilities such as this one," said Jackiewicz. "This space reflects our ongoing commitment to high quality, advanced care, as well as our focused efforts on growth and expansion."

Take campus shuttles to *L.A. Times* Festival of Books



This year's *Los Angeles Times* Festival of Books at the University of Southern California runs April 21-22 at the University Park campus.

USC's Intercampus Shuttle will provide service between the University Park campus, Union Station and the Health Sciences campus throughout the festival.

Pick-up and drop-off for the University Park campus will be on Jefferson Blvd. at Hoover St. Pick-up and drop-off for the Health Sciences campus will be on Eastlake Ave. at San Pablo Ave.

The shuttle will leave the University Park campus approximately every 30 minutes from 8:30 a.m. to 8 p.m. on Saturday, and from 8:30 a.m. to 7 p.m. on Sunday.

For more information, visit: http://tinyurl.com/yekqwvy.

KORNBERG: Nobel Leaureate visits Keck School of Medicine

Continued from Page 1

was discovered through examining yeast cells: researchers found a mediator complex that was common to all cells with membranes, not just to yeast cells. "Mediator complexes interact directly with polymerase II, and are essential in the chain of communication," Kornberg said. "Mediator mutations can cause transcription errors ranging from loss of flowers in plants to colon cancer in humans."

Kornberg's last visit to USC was in 2003, when he was awarded the Massry Prize. He is one of only six pairs of father/son Nobel Prize winners; his father, Arthur Kornberg, was awarded the Nobel Prize in Physiology or Medicine in 1959 for studies of how genetic information is transferred from one DNA molecule to another.

This visit to the Keck School included a lunch with 12 Keck School students and Dean Carmen A. Puliafito. "We thank Dr. Kornberg for his generous contribution of time to meet with our faculty, students and postdocs," Puliafito said.

To view the archived webcast of Kornberg's lecture, visit http://tinyurl.com/85j9h2u.

Ryan Ball

Nobel Prize winner Roger Kornberg of the Stanford University School of Medicine delivers his April 10 lecture at Mayer Auditorium

USC research suggests Viking landers found life on Mars

By Leslie Ridgeway

In 1976, the National Aeronautics and Space Administration (NASA) launched the Viking program, sending space probes to Mars to determine whether there was life on the red planet. Thirty-six years later the debate about life on Mars is not over, but research conducted in part at USC offers more proof that life may exist on this neighboring world.

Joseph D. Miller, associate professor of cell and neurobiology at the Keck School of Medicine of USC, and colleagues conducted an independent analysis of the labeled release (LR) data from the Viking 1 and 2 landers. The researchers applied mathematical measures of complexity to the data, which indicate a high degree of order that is more characteristic of a biological rather than a non-biological, purely physical process.

The research was published online April 9, 2012, in the *International Journal of Aeronautical and Space Sciences*.

In the experiments, the Viking landers dropped on Mars about 4,000 miles apart, scooped up soil samples and applied a radio-labeled nutrient cocktail to the soil. If microbes were present in the soil, they would likely metabolize the nutrient resulting in the release of carbon dioxide or possibly methane. The active experiments did indicate metabolism, and control experiments on sterilized soil samples produced little or no gas release. But due to lack of support from two other Viking experiments that did not find any organic molecules in the soil, most scientists believed the LR data had been compromised by a nonbiological oxidizing property of Mars soil.

Miller and colleagues did not accept this interpretation, and over the last six years applied measures of mathematical complexity to the data from active and control Viking data, as well as terrestrial biological and nonbiological data sets. Not only did the active Viking LR experiments exhibit higher complexity than the control experiments, but the active experiments clearly sorted with terrestrial biological data series whereas the Viking LR control data sorted with known terrestrial nonbiological data.

"To paraphrase an old saying, if it looks like a microbe and acts like a microbe, then it probably is a microbe," said Miller, who is a neuropharmacologist, but also studies circadian rhythms at USC and is an author on the research. "The presence of circadian rhythmicity and a high degree of mathematical complexity or order in the LR data most likely mean Viking discovered microbial life on Mars over 35 years ago."

Without a protective atmosphere similar to Earth's, life on Mars is more likely to exist underground, where it is safe from ultraviolet radiation, Miller said. If life does exist on Mars, the knowledge could unlock secrets of life here on Earth.

"We have only one example of life in the universe—we are it," said Miller. "Finding another example of life somewhere else could be the biggest step forward in biology since the delineation of the genetic code by Crick and Watson."

The Weekly NEWSMAKERS

An April 16 story in ***Wired*** featured cardiologist **Leslie Saxon**, professor of clinical medicine at the Keck School, and her project Everyheartbeat.org, a sort of "Facebook for medicine" that encourages patients to record and upload health data using smart phone accessories.

An April 12 report in ***National Geographic*** quoted **Joseph Miller**, associate professor of cell and neurobiology at the Keck School, about his research, which suggests that the Viking Mars landing program likely found life on Mars in 1976. The research also was featured by news outlets around the globe including ***Popular Science, Futurity***, RedOrbit, ***International Business Times***, SmartPlanet, TG Daily, Digital Journal, The State Column, ***The Huntsville Times, Asian News International***, Discovery News, ***Daily Mail*** (U.K.), ***National Post*** (Canada), Slobodna Dalmacija (Croatia), O Globo (Brazil), NTV (Turkey), Iltalehti (Finland), VnExpress (Vietnam), and Giornalettismo (Italy), among others.

An April 12 article in the ***Pasadena Star-News*** quoted **Scott Evans**, COO and interim CEO of the Keck Medical Center of USC hospitals, and **Tom Jackiewicz**, senior vice president and CEO of USC Health, in a story about the opening of a new Keck Medical Center of USC Pasadena medical office. The story also appeared in the ***San Gabriel Valley Tribune***. Evans and Jackiewicz also were quoted about the opening in an April 10 report in the ***Daily Trojan***.

The Hindu (India) ran an op-ed on April 6 by **Jay Desai**, assistant professor of clinical pediatrics at the Keck School, about plans to allow doctors with Overseas Citizens of India status to practice medicine within the country or become faculty members in Indian medical colleges.

Calendar of Events

This Calendar of Events is also online at www.usc.edu/hsccalendar for the Health Sciences campus community

Tuesday, Apr. 24

Noon. USC Global Health Lecture Series. "A Struggle for Relevance: The Future of WHO," Kelley Lee, London School of Tropical Medicine. Lunch will be served. UPC: TCC 450. Info: (323) 865-0419

Wednesday, Apr. 25

Noon. ZNI Seminar. "The Role of Inhibitory Circuits in Cerebellar Cortical Processing," Court Hull, Harvard. ZNI 112. Info: (323) 442-2144

Noon. TSRI Research Seminar. "Training Pediatric Researchers," Hugh O'Brodovich, Stanford. CHLA Saban Building Auditorium. Info: (323) 361-2278

Thursday, Apr. 26

10 a.m. – 2 p.m. Image Enhancement Center Open House. The center's specially trained staff provides cancer patients the techniques and encouragement necessary to help patients maintain a positive self-image. USC Norris Cancer Hospital First Floor. Info: (323) 865-3169

Noon. Dean's Translational Medicine Seminar. "Fostering Innovation and New Medical Device Development in Academic Medical Centers: The University of Michigan Medical Innovation Center Experience," James Geiger, Univ. of Michigan. MCH 149. Info: (323) 442-7732

Friday, Apr. 27

8 a.m. Pathology and Laboratory Medicine Grand Rounds. "Expression of SMARCB1/IN11," Alexander Judkins, CHLA. NOR 7409. Info: (323) 442-1180

8:30 a.m. Research Seminar. "Alveolar Epithelial Cell Dysfunction in IPF: The Role of Endoplasmic Reticulum Stress," William Lawson, Vanderbilt. IRD 732-734. Info: (323) 442-7732

Noon. Center for Applied Molecular Medicine. "Microfluidics for Cancer Cell Chemotaxis," Mingming Wu, Cornell University. CSC 250. Info: (323) 442-3849

Sunday, Apr. 29

3 p.m. KSOM Orange County Reception: Dean Puliafito hosts the OC Trojan Family and introduces the newly appointed director of the USC Norris Comprehensive Cancer Center, Stephen Gruber. Balboa Bay Club, 1221 West Coast Highway, Newport Beach, CA 92663. To RSVP: keck.usc.edu/balboabayclub Info: (323) 442-1767

Monday, Apr. 30

Noon. KSOM Research Seminar. "Vault Nanoparticles: A Platform Technology for Therapeutic Delivery and Vaccine Development," Leonard Rome, UCLA. NRT Aresty Auditorium. Info: (323) 442-7732

Saturday, May 12

7 a.m. – noon. Revlon Run/Walk For Women at Los Angeles Memorial Coliseum at Exposition Park. The cost to run/walk is $35 through May 11 ($40 day of the event). Your registration fee includes an EIF REVLON Run/Walk for Women T-shirt and goodie bag. It will also include a USC Norris Team T-shirt. Info: (323) 865-0668

Notice: Deadline for calendar submission is 4 p.m. Monday to be considered for that week's issue—although three weeks' advance notice of events is recommended. Please note that timely submission does not guarantee an item will be printed. Send calendar items to *The Weekly*, KAM 400 or fax to (323) 442-2832, or email to eblaauw@usc.edu. Entries must include day, date, time, title of talk, first and last name of speaker, affiliation of speaker, location and a phone number for information.

Martha Benedict

USC program helps healthful eating habits take root at local elementary school

Lauren Cook (center right) of the USC Childhood Obesity Research Center (USC-CORC) helps fifth graders during a cooking demonstration at the Monte Vista Elementary School Garden Celebration and LA Sprouts Open House on March 27.

A garden was planted at the school as part of the LA Sprouts program, a collaboration with USC-CORC, the UCLA Fielding School of Public Health and other community partners.

USC-CORC researchers hope the intervention program will curtail childhood obesity and resulting health problems by encouraging kids to connect with food by growing and cooking it. LA Sprouts expects to add other schools in the future.

Keck School study sheds light on cells that help heal liver

By Robin Heffler

USC researchers have identified cells that can initiate healing of a damaged liver, which promises to help physicians find treatments for acute liver disease and liver failure.

Laurie D. DeLeve, a Keck School of Medicine of USC professor and associate chair for scientific affairs in the Department of Medicine, was the principal investigator of "Liver sinusoidal endothelial cell progenitor cells promote liver regeneration in rats," which was published on March 12 in the online version of *The Journal of Clinical Investigation*. Joining her in the research was Lin Wang, a postdoctoral student from the Fourth Military Medical University in Xi'an, China.

The liver, which detoxifies chemicals, metabolizes drugs and makes proteins important for blood clotting and other functions, is the only solid organ that has the ability to regenerate after it has sustained significant tissue damage and even after partial surgical removal.

With funding from the National Institutes of Health, DeLeve and her colleagues from the USC Research Center for Liver Diseases sought to pinpoint specific cells that are needed for such regeneration.

"Through animal models, we showed that liver regeneration requires the recruitment of these bone marrow progenitor cells," she said. "The results also may shed light on liver complications in patients with bone marrow suppression." Suppression of bone marrow function can be a serious side effect of chemotherapy and certain drugs, and is seen in various diseases.

In the most recent research, DeLeve's team discovered that after partial surgical removal of rat livers, cells from the bone marrow are recruited to the liver and repopulate the vascular lining of the organ.

The recruited bone marrow cells are called progenitor cells, and are the offspring of stem cells. Once lodged in the liver, the progenitor cells become liver sinusoidal endothelial cells, the specialized cells that line the liver's vascular system and perform a variety of functions. These progenitor cells also are a major source of hepatocyte growth factor, which stimulates liver cell proliferation when a portion of a rat's liver is removed.

The study demonstrated that without recruitment of these bone marrow progenitor cells, the liver is not able to regenerate normally.

DeLeve's laboratory is now investigating the various signals that regulate how progenitor cells are recruited from the bone marrow.

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