Featured Member: Jinxi Wang, MD, PhD

Dr. Jinxi Wang’s research has gained national and international recognition. Currently, he serves as a grant reviewer for two NIH study sections and a DoD grant review panel. He also serves as an editorial board member for several national and international biomedical journals, and is a member of the New Investigator Mentoring Committee of the Orthopedic Research Society (U.S.A).

Dr. Jinxi Wang received his medical degree from Suzhou Medical College in China and his PhD degree and orthopedic residency training from a joint program of Suzhou Medical College and Loma Linda University in California, followed by postdoctoral research training in molecular and cellular biology of the skeletal system at Harvard University Medical School. His basic science and clinical training background enables him to effectively integrate basic sciences with clinical applications.

Dr. Wang held a junior faculty position in Orthopedics at Harvard Medical School and Boston Children’s Hospital from 1997 to 2005. He joined the University of Kansas Medical Center (KUMC) in 2005 as an Associate Professor of Orthopedic Surgery and the designated heir to the Harrington Professorship, with a major mission to develop a new skeletal...
biodiversity laboratory in the Department of Orthopedic Surgery. This laboratory was named “The Harrington Laboratory for Molecular Orthopedics” in accordance with Dr. Harrington’s wishes. Dr. Wang was invested with the Mary A. and Paul R. Harrington, MD, Distinguished Professorship in 2011 after a rigorous evaluation of his contributions to the development of the Harrington Laboratory and research program in molecular orthopedics.

Dr. Wang and his research team have developed a research program in the areas of skeletal biology and pathology over the past 8 years. Specific research interests include: 1) regulatory mechanisms of osteoblast differentiation and bone regeneration, 2) chondrocyte differentiation and articular cartilage regeneration, and 3) pathogenetic mechanisms and novel therapies for osteoarthritis. Idiopathic or post-traumatic osteoarthritis (OA) is the most common form of joint disease. No proven pharmacologic therapy is currently available to prevent the initiation or reverse the progression of OA, largely because the pathogenetic mechanisms of OA remain unclear. Previous studies suggested that overexpression of specific proinflammatory cytokines and matrix-degrading enzymes may cause joint cartilage degradation. A large number of candidate anti-OA drugs targeting a single proinflammatory cytokine or matrix-degrading enzyme have been tested through clinical trials but none have been approved due to insufficient efficacy, suggesting that a candidate anti-OA drug based on inhibition of a single catabolic enzyme or cytokine is unlikely to produce long-term benefits. Dr. Wang’s research group has recently discovered that the transcription factor NFAT1 is a key factor that regulates the expression of multiple catabolic enzymes/cytokines and anabolic factors in adult joint tissues (e.g., articular cartilage and synovium). NFAT1 is a critical factor for maintaining the balance between anabolic and catabolic activities in the articular cartilage. NFAT1 deficiency causes OA in adult mice and is associated with a subset of human subjects with OA. This discovery provides a better understanding of the pathogenesis of OA and opens a new avenue towards the development of effective strategies for prevention and treatment of OA.

These research projects are currently supported by the Harrington Distinguished Professorship Endowment, three NIH (National Institutes of Health) R01 grants, and a DoD (U.S. Department of Defense) grant.
Members In the News

KU family medicine professor Sarah Kessler is working to slow the spread of HIV and AIDS in Africa

December 10, 2012
By Aubrey Bittel

Few global health issues are more urgent or devastating than the toll of HIV and AIDS in Africa. Sub-Saharan Africa has 10 percent of the world’s population but is home to 70 percent of people living with HIV and AIDS. And according to the UNAIDS Report on the Global AIDS Epidemic, 72 percent of those who died from AIDS and its complications in 2010 lived in Africa.

Sarah Kessler, Ph.D., MPH, an assistant professor in KU Medical Center’s Department of Family Medicine’s research division, is committed to helping slow the spread of HIV, particularly in Africa, by decreasing the number of infants born with the disease. Kessler, who has spent time researching HIV in the United States, Kenya, and Uganda, says that understanding the culture is key to helping any community combat the disease. For example, in some Kenyan and Ugandan communities all women are expected to bear children at some point.

“That’s part of their culture,” Dr. Kessler says. “It’s unheard of for a woman to choose not to have children, and that mindset often doesn’t change if the woman or her husband is HIV positive.”

Kessler, who recently received a grant to provide Ugandans with safer childbearing techniques, advises men and women how they can reduce the risk of spreading the virus to their babies.

“It’s possible to significantly reduce the risk of the child contracting the virus with treatment. If the medication is taken regularly, there’s less than a 1 percent chance that HIV-positive parents will have an HIV-positive baby.”

If an infant does test positive for the disease, he or she is not necessarily doomed to a short and painful life. The mortality rate of HIV-positive infants decreases by 76 percent when they begin treatment by 12 weeks of age. Problems begin when obstacles arise between children and treatment, and this is where Kessler sees potential for improvement. She is currently working with Brad Gautney, president of Global Health Innovations and founder of the HIV Infant Tracking System, (HITSystem) to improve communication between laboratories, health care providers and patients. Currently piloted in four hospitals in Kenya, the HITSystem moves patients’ medical records from volumes of manually entered information to an online infrastructure.

Continued on page 4
“The current system for many hospitals is a very large notebook,” Kessler explains. “Pages will be missing, there are stains, it’s all hand-written, and it’s very difficult to read it.”

The HITSystem allows health care providers to enter a patient’s history directly into the online database. Vital information such as whether the mother took antiretroviral drugs during pregnancy is now available not only to the health care providers, but also to the lab technicians who will be testing the child’s blood samples for the disease. Currently, these samples and the test results are physically transported from the health care provider to the laboratory and back, and it is common for them to be misplaced in transit. With the HITSystem, lab workers enter results electronically, and providers immediately see them. Mothers concerned about their babies’ HIV status no longer need to worry that they will not receive results. The providers have them as soon as they are entered. Additionally, the HITSystem includes an alert if information is not entered when necessary.

“We allow the laboratory 10 days with a sample,” Kessler says. “If we don’t get that result posted, they get an alert and know they need to resolve that.”

Another aspect of the HITSystem in the Kenyan pilot study is direct communication with the child’s family. Kessler and her colleagues have found that maintaining contact with the mother improves the chances they will return for follow-up care. The most effective form of communication usually depends on economic conditions. In the country’s urban areas, where two of the pilot’s studies are located, 97 percent of the mothers involved in the study have access to cell phones. In those areas, texting has proved an effective tool to alert mothers of upcoming test results or medical appointments. In the other two hospitals, which are located in more rural areas, only 63 percent of the patients reported having access to cell phones. In those areas it has been necessary for health care officials to make trips to different communities to deliver medical information. Luckily, the HITSystem also makes it easier to track patients’ locations, enabling officials to successfully reach more people.

Kessler has recently helped submit an National Institutes of Health research project grant to expand the HITSystem to Malawi, one of the African countries most affected by HIV/AIDS. It is also a much more agriculturally focused and rural country. Cell phones are extremely uncommon. This poses an even bigger challenge, but Kessler is excited about the challenge.

“Malawi is where this program could have a really big impact,” she says. “There are so many HIV-positive babies that are not getting linked to care.”

You can learn more about the HITSSystem, or make a charitable donation by visiting http://globalhealthinnovations.org/.
One of these stem cells is not like the other” – KU Medical Center researcher Jay Vivian asks why

January 07, 2013
By Alissa Poh

When stem cells were first generated from human skin in the laboratory five years ago, scientists rejoiced. At long last, they could employ a highly-coveted characteristic of naturally-occurring stem cells — pluripotency, or the ability to become different cell types — in regenerative medicine, while bypassing a host of ethical issues associated with using embryonic stem cells. For their seminal research, some 40 years apart, that made these lab-created cells, called induced pluripotent stem (iPS) cells, possible, Sir John B. Gurdon and Shinya Yamanaka shared this year’s Nobel Prize in Physiology or Medicine.

Jau L. Vivian, PhD

It turns out, however, that for all their great therapeutic potential, iPS cells — and probably stem cells in general — have something in common with teenagers: they’re often unpredictable.

“In a perfect world, we could direct a dish of pluripotent stem cells to differentiate, or turn into a specific kind of cell, and they’d do so in lockstep,” says Jay Vivian, Ph.D., an assistant professor in the Department of Pathology and Laboratory Medicine at the University of Kansas Medical Center. “But nothing’s perfect in science, and we usually end up with an ugly mess of stuff — some of the cells that we want, and a lot more that we don’t.” A member of KU’s Institute for Reproductive Health and Regenerative Medicine, Vivian is trying to work out why these cells are more difficult to manipulate than previously imagined, and recently published a paper on this topic in the October 2012 issue of the journal Stem Cells.

The starting point, Vivian says, is overcoming the assumption that pluripotent stem cells are all alike. On the contrary, they don’t behave in identical fashion and often don’t even look the same. “They’re heterogeneous,” he says, which is science lingo for “not uniform.” The cells are also dynamic, able to wander in and out of different states seemingly at will. And yet it isn’t random, as he and his group explain in their research, which zeroes in on three of the molecular players responsible for driving these dynamic differences.

Meet Nanog, Nodal and a third character more broadly known by its initials: BMP. Nanog is a master regulator and, Vivian says, “absolutely required” for stem cells to display pluripotency. Nodal and BMP both belong to a large group of signaling molecules called the TGF-beta superfamily. Each sets in motion a different chain of activities that ultimately regulates the overall process of transcribing individual genes into proteins.

“Here’s the conundrum,” Vivian says. “Nanog controls thousands of genes that keep cells pluripotent, or in an undifferentiated state. But pluripotent cells don’t all have the same amount of Nanog. In fact, it’s highly variable. We divvied them up into four groups - cells with very
high, high, medium or low Nanog levels - and asked, ‘Why these differences, given Nanog’s importance?’

In the laboratory, Vivian suppressed Nodal’s signaling pathway in mouse embryonic stem cells and saw that their shape changed. “They became very round and tightly clumped,” he says. “These mouse ES cells like sticking together anyway, but became even more cohesive when Nodal signaling was switched off.”

In a separate experiment, Vivian tagged Nanog so it glowed fluorescent green and tracked its levels in mouse cells. He noted that cells with higher amounts of Nanog resembled cells in which Nodal signaling was suppressed: tight and round. “But Nanog-low cells were somewhat flatter, with poky little edges to them,” he says. “We wondered if these two observations were related, and Nodal and Nanog were communicating with each other. Sure enough, that turned out to be the case.”

By teasing apart the conversational tangles, Vivian and his group found that Nodal talks to Nanog through BMP. Normally, BMP oversees a group of proteins collectively named Id, but Nodal interacts with and lowers BMP’s signaling activity. “Id proteins heavily influence a cell’s decision to have high or low Nanog expression,” Vivian explains. “If Nodal is blocked, BMP’s activity increases, which in turn pushes cells to a Nanog-high state.”

“We’ve defined the molecular hierarchy at play here,” he adds, “all because of a simple observation under the microscope: ‘Some of these cells look a little funny.’”

Vivian says heterogeneous pluripotent stem cells are sort of like a mixed bag of M&M’s. “Think of cells with very high Nanog levels as green M&M’s, the ones with medium levels as yellow M&M’s, and Nanog-low cells as those brown M&M’s most people don’t want to eat,” Vivian says. But because the differences are dynamic, the candy is really more like the magical sweets Harry Potter and his friends consumed at Hogwarts: brown M&M’s can turn green, and vice versa.

“Functionally, Nanog-high cells are much better to work with, so we want to learn more about other factors that influence a cell’s decision to exist in this particular state,” Vivian says. “We want more green M&M’s, basically.”

Mouse embryonic stem cells were part of this research because, Vivian explains, “they’ve been studied for 25 years and we know a lot more about working with them, compared to human iPS cells.” But he and his crew are using iPS cells more, focused on directing their differentiation into neural cells that could be used to treat spinal cord injuries. “I believe what we’ve learned with our mouse work can be extrapolated,” Vivian says, “because heterogeneity also exists in iPS cells, and I’m pretty sure Nodal and BMP, at least, are influencing factors.”

Vivian emphasizes that the use of pluripotent stem cells in regenerative medicine is still very much in its infancy. “We don’t yet fully understand just how complex these cells are, much less everything that influences them to differentiate or remain in their original state,” he says. “Once we have a clearer picture of how heterogeneity is established and how it might be tinkered with, we can better direct these cells toward becoming the types we want, therapeutically.”
Some Recent Publications


FACULTY AWARDS

PI: Kenneth R. Peterson, PhD
NIH Roadmap Molecular Libraries and Imaging Division of Neuroscience and Basic Behavioral Science National Institute of Mental Health, 1 X01 MH100830-01
“HTS for HbF Inducers in Human Beta-globin YAC Transgenic Mice Bone Marrow Cells”, 1/11/13-1/10/14

PI: Merlin G. Butler, MD, PhD, FFACMG
National Health and Medical Research Council (NHMRC) of Australia

PI: Merlin G. Butler, MD, PhD, FFACMG
Prader-Willi Syndrome Association (USA)
This competitive support arises from the NIH Rare Disease Grant U54HD061222 06 to support research activity of a young investigator to engage in the study of rare diseases.
“RDCRN Fellowship Support to Study Rare Diseases including Prader-Willi Syndrome”, 2012

PI: Jinx Wang, MD, PhD
U.S. Department of Defense (DoD), W81XWH-1210304
“Deficiency of NFAT1 Transcription Factor and Post-Traumatic Osteoarthritis”, 08/01/2012 – 07/31/2015

PI: Kathleen M. Gustafson, PhD
Mead Johnson Nutritionals
“State of the Art ERP Analysis of EEG Data from the DIAMOND Study”, 9/2012-8/2013

PI: Julie A. Carlsten Christianson, PhD
NIH/NIGMS
“Impact of Early Experience on Vulvovaginal Sensitivity in Adult Mouse” 9/1/2012-6/30/2014

PI: Rajasingh Johnson, M.Phil., PhD, HCLD
NIH supported clinical and translational science ward-Frontiers Pilot Grant

FACULTY HONORS/AWARDS

Merlin G. Butler, MD, PhD, FFACMG – 2012 Consumers’ Research Council of America, Guide to America’s Top Physicians

Ann Manzardo, PhD, MSCR - 2012 New Investigator Award Recipient, NIH Rare Disease Clinical Research Network (RDCRN) (Prader-Willi, Angelman, and Rett syndromes) (Merlin G. Butler, MD, PhD, FFACMG – Mentor)

Michael Wolfe, PhD – Appointed KUMC Research Integrity Officer

Warren Nothnick, PhD - Appointed Scientific Director of Lab Animal Resources (LAR)

Continued on page 9
**Honors/Awards (Cont. from pg 8)**

Jinxi Wang, MD, PhD - August 2012, NIH Study Section Special Emphasis Panel: Skeletal Pathology and Orthopedics

Jinxi Wang, MD, PhD - September 2012, U.S. Department of Defense (DoD) Peer Reviewed Medical Research Program Peer Review Panel

Jinxi Wang, MD, PhD - February 2013, NIH Study Section: Skeletal Biology Development and Disease (SBDD) Study Section

### TRAINEE HONORS/AWARDS

Chad Walesky (Udayan Apte Lab)  
First Place in Platform Presentation at the Central States Chapter of The Society of Toxicology

Bharat Bhushan (Udayan Apte Lab)  
Second Place in Poster Presentation at the Central States Chapter of The Society of Toxicology

Pengli Bu (Michael J. Soares Lab)  
Lalor Foundation Travel Award to the 2012 Annual Society for the Study of Reproduction Meeting in State College, Pennsylvania

Kaiyu Kubota (Michael J. Soares Lab)  
Recipient of a Best Poster Award at the 2012 Annual Greenwald Symposium on Reproduction

Lei Qiu (Adam Krieg Lab)  
Recipient of a Best Poster Award at the 2012 Annual Greenwald Symposium on Reproduction

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**Highlights: Upcoming Events**

**The 10th Annual Gilbert S. Greenwald Symposium on Reproduction and Regenerative Medicine**

**SAVE THE DATE:**  
October 17-18

The 10th Annual Gilbert S. Greenwald Symposium on Reproduction and Regenerative Medicine is scheduled for Thursday and Friday, October 17-18, 2013.

Approximately 100 faculty, trainees and staff participated in last year’s event, which was held October 11-12, 2012. This year’s format and schedule will be similar to last year’s, with KUMC as the venue for the Thursday events and the Kansas City Public Library-Central as the venue for Friday.

**We look forward to this year’s exciting line-up:**

**Keynote Address:**

Martin M. Matzuk, MD, PhD,  
Baylor College of Medicine

**Plenary Lectures:**

Frederick vom Saal, PhD,  
University of Missouri-Columbia

Mary Hunzicker-Dunn, PhD,  
Washington State University

*Continued on page 10*
The Annual Donald C. Johnson Lecture in Reproduction

SAVE THE DATE: May 16

Günter P. Wagner, PhD from Yale will be giving this year’s Annual Donald C. Johnson Lecture in Reproduction on May 16 at 8:30 a.m. in the Lied Auditorium, titled “The Endometrial Stromal Cell: The Molecular Evolution of a Major Evolutionary Novelty”.

This lectureship honors the reproductive biology research career of former KUMC faculty member Donald C. “DC” Johnson (pictured left).

For more information, visit our website
http://www.kumc.edu/school-of-medicine/irhrm/events/donald-c-johnson-lecture.html

The Annual James L. Voogt Lecture in Neuroendocrinology

SAVE THE DATE: May 9

P. Michael Conn, PhD from Oregon Health and Science University will be giving this year’s Annual Voogt Lecture in Neuroendocrinology on May 9 at 8:30 a.m. in the Lied Auditorium, titled “Pharmacoperones: A New Therapeutic Approach Unfolding”.

This lectureship honors Dr. James L. Voogt, an emeritus faculty member of KUMC whose research career focused on Neuroendocrinology. Dr. Voogt will be present at the lecture, and we hope you will join us!

For more information, visit our website
http://www.kumc.edu/school-of-medicine/irhrm/events/james-l-voogt-lecture.html

Visit us online for event updates, news highlights and more!

www.kumc.edu/irhrm

Please direct questions, comments and suggestions to

Stacy McClure
913-588-5774
smcclure@kumc.edu
## Upcoming Events (February - May, 2013)

### February 2013

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<tr>
<th>Date</th>
<th>Event</th>
<th>Location</th>
<th>Speaker(s)</th>
<th>Title</th>
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<tr>
<td>6</td>
<td>CRS Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Peter Smith, PhD</td>
<td>Neuroplasticity of the Female Reproductive Tract</td>
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<tr>
<td>13</td>
<td>CDOHAD Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Holly Hull, PhD</td>
<td>Novel Methods to Prevent Excessive Gestational Weight Gain in Overweight Women</td>
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<td>20</td>
<td>CESCB Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Jinxi Wang, MD, PhD</td>
<td>Epigenetic Regulation of NFAT1 Expression in Articular Chondrocytes and its Implications in Osteoarthritis</td>
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### March 2013

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<tr>
<td>5</td>
<td>CRS Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Gustavo Blanco, MD, PhD</td>
<td>The Testis Specific Na,K-ATPase Alpha4 Isoform is Essential for Male Fertility</td>
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<tr>
<td>7</td>
<td>Seminar</td>
<td>Lied Aud., Noon, 8:30-9:30 am</td>
<td>Jason Knott, PhD</td>
<td>Emerging Roles of Tcfap2c and Brg1 During Early Embryogenesis in the Mouse</td>
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<td>13</td>
<td>CDOHAD Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Kelly Bosak, PhD</td>
<td>Neuroimaging of Goal-directed Behavior in Overweight Women</td>
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<td>20</td>
<td>CESCB Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Chad Slawson, PhD</td>
<td>The Regulation of Growth and Development by O-GlcNAc</td>
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<td>28</td>
<td>Seminar</td>
<td>Lied Aud., Noon, 8:30-9:30 am</td>
<td>Jodi Flaws, PhD</td>
<td>Effect of Endocrine Disrupting Chemicals on the Mammalian Ovary</td>
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### April 2013

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<tr>
<td>3</td>
<td>CRS Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>M.A. Karim Rumi, MD, PhD</td>
<td>Targeted Esr1 Knockout in Rats Using Zinc Finger Nuclease-Mediated Genome Editing</td>
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<td>10</td>
<td>CDOHAD Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Carl P. Weiner, MD, MBA</td>
<td>Title TBD</td>
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<tr>
<td>17</td>
<td>CESCB Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Rajasingh Johnson, MPhil, PhD, HCLD</td>
<td>Reprogramming of Human Somatic Cells into Cardiac Progenitor Cells</td>
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<td>18</td>
<td>Seminar</td>
<td>Lied Aud., Noon, 8:30-9:30 am</td>
<td>Lindsay E. Hinck, PhD</td>
<td>Basal Cells and Growth Control in the Breast</td>
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<td>24</td>
<td>CRS Chalk Talk</td>
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<td>Adam Krieg, PhD</td>
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### May 2013

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<td>1</td>
<td>CRS Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Brian Petroff, DVM, PhD</td>
<td>Challenges of Cancer Prevention</td>
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<td>2</td>
<td>Seminar</td>
<td>Lied Aud., Noon, 8:30-9:30 am</td>
<td>Jurrien Dean, MD</td>
<td>Maternal Matrices in Fertilization and Early Development</td>
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<td>8</td>
<td>CDOHAD Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Gene Lee, MD</td>
<td>Title TBD</td>
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<tr>
<td>9</td>
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<td>CESCB Chalk Talk</td>
<td>HLSIC, Noon, 3070</td>
<td>Hao Zhu, PhD</td>
<td>Ncb5or-dependent Iron Homeostasis in Beta-cell Function and Survival</td>
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<td>Seminar</td>
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<tr>
<td>30</td>
<td>Seminar</td>
<td>Lied Aud., Noon, 8:30-9:30 am</td>
<td>Markus Grompe, MD</td>
<td>Liver Cell Transplantation</td>
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Sculpture: “Stemmer No. 7”, by David Fried, 2005