‘Rules in Science’

Stem Cell Innovator Yamanaka Shares Secrets of Success
By Carla Garnett

Not too long ago, a mild-mannered scientist from Japan was tending his own lab animal cages. He had no lab techs and no funds to hire any. Next thing he knew, he was becoming famous worldwide for a stem cell breakthrough so stunning the research community is still gasping. At least that’s the way Dr. Shinya Yamanaka, director of the Center for iPS Cell Research and Application, Kyoto University, told his story Jan. 14 to an SRO crowd in Masur Auditorium. Of course, he shared the groundbreaking technique for making all-purpose stem cells without using embryos. But more, he gave the audience a rare and humorous glimpse

Dr. Shinya Yamanaka spoke at NIH on Jan. 14.

Knitter Power

Rosenberg Launches Cap Campaign to Save Newborns
By Belle Waring

A baby’s first cry is a sound like none other. We know that infants must learn to breathe on their own, and fast. And they must also survive being pushed from the perfection of their mothers’ warmth.

To be expelled, soaking wet, not wearing a stitch, suddenly exposed to room temperature, or worse—what a shock.

Here’s the problem: The newborn brain is too immature to maintain body temperature. Even a healthy, full-term infant has few defenses against cold stress.

That’s why delivery room nurses slip stockinette caps onto newborn heads. The scalp has a relatively large surface area from which heat can be lost and if an infant’s temperature dips too low for too long, cold injury can trigger a chain reaction that ends in death.

“Understand that people live in a world where a baby can die of cold,” says NIAID’s Alice Rosenberg. “In Rwanda, a man walked for 3 days with his pregnant wife in a wheelbarrow to bring her to a clinic only to have the baby die of hypothermia.”

Now, at the request of Dr. Paul Farmer and his nonprofit orga-
briefs

STEP Forum on Social Networking Tools

The staff training in extramural programs (STEP) committee will present an Administrative Strategies forum on the topic “Blogspot and Facebook and Twitter, Oh My! The Potential of Social Networking Tools for Public Health Research” on Tuesday, Mar. 9, from 8:30 a.m. to 12:30 p.m. in Lister Hill Auditorium, Bldg. 38A.

It is challenging to keep up with the lingo and the technology provided by the Internet. Experts talk about the immense opportunity for commerce and knowledge transfer—how can scientists get in on the action? This forum will present the latest Internet-based social networking developments and how researchers can use these technologies to expedite interdisciplinary communication, expand knowledge and reach a potentially untapped population. Come tweet with us!

HHS Mentoring Program Recruits

NIH wants you to join the HHS Mentoring Program. Permanent federal employees interested in serving as mentors and mentees across the NIH community are invited to join the NIH April 2010 cohort.

Building a confidential, interactive relationship is the cornerstone of the program. The program's emphasis on developing leadership and management competencies at various levels will ensure a beneficial experience for both mentors and mentees.

Program components include:
- senior-to-junior and peer-to-peer mentoring relationships
- online application and matching system to connect individuals
- mentor-mentee online orientation
- 1-year mentoring relationship commitment
- professional development events and activities

As a tool in employee development, the HHS Mentoring Program does not supplant the NIH scientific mentoring and customized IC leadership mentoring programs that are available to employees in some institutes and centers. Instead, it fills an existing need and enables NIH-wide or department-wide relationships. For more information, including links to online registration and upcoming information sessions, visit http://trainingcenter.nih.gov/hhs_mentoring.html.

NIH Golf Association Seeks New Members

The NIH Golf Association (18-hole competitive coed league) is looking for new members for the 2010 season. It currently has 7 teams of up to 25+ players each and schedules 8 stroke play outings in the spring and summer. Stroke play is followed by up to 5 match play outings. All outings are mid-week at local courses in Virginia and Maryland and play is optional. The NIHGA caps the year off in October with an outing that includes golf/cart and dinner for all members and their guests. Prizes and trophies are awarded and handicaps are maintained from 0-40, so all golfers are welcome. For more information contact Howard Somers at somersh@mail.nlm.nih.gov; visit www.recgov.org/nihga/ for complete information on the upcoming schedule and other news.

NCI Holds Biospecimen Research Network Symposium, Mar. 24-25

Save the date for the National Cancer Institute’s 3rd annual Biospecimen Research Network Symposium, “Advancing Cancer Research Through Biospecimen Science,” Mar. 24-25 at the Bethesda North Marriott Hotel & Conference Center. The symposium will address the significant impact of pre-analytical biospecimen variables on cancer research and molecular medicine. Hosted by NCI’s Office of Biorepositories and Biospecimen Research, the meeting will bring together leaders in the fields of biospecimen research, genomics, proteomics, oncology, pathology, biobanking, hospital administration and pharmaceutics as well as patient advocates. The 2-day event will feature presentations and interactive discussions about biospecimen quality. Visit http://brnsymposium.com/meeting/brnsymposium/2010/ to get the latest information about speakers, topics and participation. Registration is now open.

IHS Director Visits NIGMS Council

Indian Health Service director Dr. Yvette Roubideaux (l) recently met with the National Advisory General Medical Sciences Council to discuss the Native American Research Centers for Health Program. This program, a partnership led by the Indian Health Service and NIGMS, develops opportunities for research and research training to meet the needs of American Indian/Alaska Native communities. Also shown are NIGMS director Dr. Jeremy Berg (c) and NIGMS associate director for extramural activities Dr. Ann Hagan.
The close of 2009 marked another successful milestone for the Heart Truth Champions Program. The 89 champions trained last year made up the largest “graduating class” since the program’s inception in 2006. The program, funded by NHLBI and the HHS Office on Women’s Health (OWH), provides a day of training for women and men to help them develop and implement local education and awareness programs on heart disease, the No. 1 killer of women in the United States. Since it began, the program has trained 214 champions in 16 cities and 14 states.

Champions take a leading role in creating opportunities for women and men to engage in community activities to spread the Heart Truth’s key messages. Sponsored by NHLBI, the Heart Truth is a national awareness campaign for women about heart disease. In 2008 alone, the Heart Truth Champions planned and conducted a total of 96 events, which reached more than 25,000 people nationwide.

The day-long training includes an overview of heart disease by a local cardiologist and/or nurse; personal stories of women with heart disease; an overview of the Heart Truth Campaign and its centerpiece—the Red Dress—designed to build awareness that women are at risk for heart disease; and an overview of education materials for the public and health professionals. The latter part of the day is designated for the group audit where the champions collectively brainstorm and identify Heart Truth-related activities or programs they hope to start within their communities.

“The Champions Program is unique because it presents a forum where women and men who are already active within their communities can come together to encourage a greater understanding of heart disease—their training spurs advocacy within their communities and a greater understanding and recognition of heart disease,” said Dr. Ann Taubenheim, chief of the Health Campaigns and Consumer Services Branch, NHLBI.

Training sites for the program are selected to target populations at high risk for heart disease based on a review of the Centers for Disease Control and Prevention’s morbidity and mortality report and Behavioral Risk Factors Surveillance System as well as target states selected by OWH. Each program is tailored to the community where the training is held.

John McQuitty, Detroit champion and volunteer minister, was interested in participating because he wanted a better understanding of heart-related health issues that affect members of his community. “I spend a good amount of time visiting members of my religious community in the hospitals so I wanted to have a better idea of the health-related challenges that they face,” he said. “I never recognized or contemplated the difference between heart disease that is inherited and heart disease that is a result of risk factors.”

Last fall, training sessions were held in Baltimore, Wilmington, Del., Cleveland, Memphis, Detroit, Louisville and Buffalo. On Feb. 5, champions led their communities in participating in National Wear Red Day. To learn more, visit www.hearttruth.gov.
into the sometimes hard-knock life of a fledgling bench scientist. And he offered every hardworking but frequently frustrated postdoc a reason to stick with research as a career.

"It’s not very many times you remember where you were when you read a particular scientific paper," said NIH director Dr. Francis Collins, introducing Yamanaka, the guest speaker at a special Thursday edition of the Wednesday Afternoon Lecture Series. "I remember where I was [in August 2006] when I read [Kazutoshi] Takahashi and Yamanaka…I was at the beach. I was supposed to be getting away from the scientific hubbub, but I’d heard that there was this paper that really ought to be looked at. There had been stories flying around in the rumor mill that a Japanese group had come up with a truly dramatic way to reprogram cells...As I read that paper, I had the hairs stand up on the back of my neck because I could see that this was transformative...The era of the induced pluripotent stem cell was born."

An Inkling Emerges

When Yamanaka took the podium next, he traveled even farther down Memory Lane, to his own postdoc days.

It was San Francisco circa 1995 and he was a former orthopedic surgeon pursuing a career in research in a Gladstone Institute lab. His PI, Dr. Tom Innerarity, had an idea involving mRNA editing that could lead to a way to lower bad cholesterol levels. In the course of the study, however, they also discovered the mice were developing huge liver tumors. APOBEC1, it turned out, is a cancer-causing gene. No way could an oncogene be used to fight heart disease.

Failure Feeds Fascination

"From this experiment I learned three important rules in science," Yamanaka quipped, smiling. "First, science is surprising. It’s difficult to predict...That’s probably why I’m still doing science. The second rule is, we should never try new procedures, new medicines, new genes directly on patients—it’s too dangerous. We should do animal studies."

Yamanaka’s third rule, "which may be the most important, is that you should not believe in your boss’s hypothesis," he joked, drawing laughter from the audience.

Although his PI was disappointed with the result of the hypothesis, Yamanaka was only further intrigued. He spent the next 3 years studying how mRNA editing enzymes cause "these ugly tumors." Eventually, Yamanaka came across another oncogene, which he named NAT1. He developed his own theory about how NAT1 influences APOBEC1 to generate tumor growth. His research was speeding along well.

Then family life intruded. His wife and young daughters relocated back to Japan, he noted with humor, leaving him hard at work in San Francisco. He soon learned another lesson: Don’t let the distance between yourself and your loved ones become too great. He missed his family.

Six months later Yamanaka returned to Japan, taking with him three elements that would play a huge role in his success story: several research mice, a hard work ethic and, perhaps most important, a now well-developed talent for genetic tinkering with NAT1.

Perseverance Pays Off

The researcher’s life in Japan was very different from what Yamanaka had grown to love in the States, however. Although he was discovering surprisingly similar biological properties in NAT1 and embryonic stem cells, Yamanaka was also suffering from a lack of scientific resources. It wasn’t long, he said jokingly, until he contracted a serious mental disorder called P.A.D.—"post-America depression."

Gone were the glory days in the U.S. when lab techs helped him care for the hundreds of mice colonies. Non-existent were funds to hire. Yamanaka was virtually alone in the lab, clean-
ing cages. Friends advised him to give up on the rodents and pursue something more useful to human health.

Disheartened both in spirit and finances, Yamanaka was about to quit science altogether “when two things rescued me from P.A.D.”

**Bold Goal as Bait**

First was Dr. Jamie Thomson’s generation of human ES cells in 1998. Second was Yamanaka’s appointment to his own lab at Nara Institute of Science and Technology in 2000. The next challenge? Populate his lab with postdocs.

Competition for talented students was fierce, Yamanaka realized. As “the newest, youngest and proudest PI,” he needed an outstanding project to entice postdocs to join his lab. He announced an ambitious long-term goal: “Make ES-like stem cells not from human embryos but from somatic cells, like skin fibroblasts, by means of reprogramming.”

It could take 30 or 40 years to accomplish this, he guessed to himself. He didn’t share that thought with the prospective protégés. Three students, including Takahashi, signed on to Yamanaka’s quest. Long story short: By 2004 the group had made unimaginable headway in just a few years. They’d reached the bold goal in less than a quarter of the PI’s estimate.

During the rest of the lecture (and at a special meeting for NIH’s Intramural Research Program held the next day in Wilson Hall), Yamanaka discussed iPS strategies and research details. He readily acknowledged many substantial obstacles yet to overcome.

The energy in Masur Auditorium was palpable. Collins had noted that many in the research community believe Yamanaka “will no doubt enjoy a trip to Stockholm sometime in the not too distant future, given the way this observation has emerged as perhaps one of the most exciting developments in science in the last decade.”

Listening to the perhaps future Nobelist—humble, humorous, brimming with enthusiasm—describe various iPS concepts, one could easily learn about more than science.

Both events with Yamanaka are archived at www.videocast.nih.gov/.

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**Nobel Laureate To Give NEI’s Sayer Lecture, Mar. 10 in Masur**

Dr. Roger Y. Tsien, winner of the Nobel Prize in chemistry for 2008, will deliver the fourth annual Sayer Vision Research Lecture on Wednesday, Mar. 10 at 1 p.m. in Masur Auditorium, Bldg. 10. His talk is titled “Breeding and Building Molecules to Spy on Cells and Tumors.”

Tsien, an investigator and professor at the Howard Hughes Medical Institute and the University of California, San Diego, was awarded the Nobel Prize for his contribution toward the discovery and development of green fluorescent protein (GFP). His work has developed GFP into a tool used by researchers worldwide to analyze the movements, positions and interactions of tagged proteins within cells. Recently, fluorescent proteins have been used to visualize synaptic circuits, allowing researchers to map glial territories and follow glial cells and neurons over time in vivo.

Tsien’s research is at the interface of organic chemistry, cell biology and neurobiology. He is best known for designing and building molecules that either report or perturb signal transduction inside living cells. He is currently designing imaging and therapeutic molecules that specifically target cancer cells.


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**Fogarty Presents Global Health Guru Rosling, Feb. 22**

Google collaborator and guru of global health data Dr. Hans Rosling will visit NIH as a Fogarty International Center scholar-in-residence on Monday, Feb. 22. Known for his humorous, yet deadly serious presentations, he will give a talk titled “The New Health Gap: Science for Emerging Economies vs. the Bottom Billion” in Masur Auditorium, Bldg. 10 at 11:30 a.m. A reception follows.

Rosling is co-founder of Gapminder, a nonprofit organization dedicated to promoting a fact-based worldview through increased use and understanding of freely accessible public statistics. Gapminder developed Trendalyzer software that converts international statistics into moving, interactive and enjoyable graphics. Google acquired the software and has expanded the effort.

Also a professor of international health at Sweden’s Karolinska Institute, Rosling co-founded Médecins Sans Frontières Sweden. While serving as a doctor in Mozambique from 1979 to 1981, he discovered konzo, a new epidemic paralytic disease. He spent the next two decades investigating the cause, which he traced to the consumption of toxic, ill-processed cassava roots combined with hunger and poverty. In addition, he has written a textbook on global health and has initiated university collaborations with Asia and Africa.

The event is sponsored by the Foundation for NIH and will be webcast.
**Baby Cap Pattern**

**Supplies:** Size #6 needles

Use washable (acrylic) baby yarn or sport weight yarn.

**Instructions:**

- Cast on the number of stitches for the size hat desired (see size chart below).
- Rib Stitch (Knit 1, Purl 1) for one inch for all sizes.
- Stockinette Stitch (Knit 1 row, Purl 1 row) for the number of inches indicated (see size chart below).
- Draw yarn through all stitches on needle. Pull tightly on top. Knot securely.
- Weave together seam using yarn.
- Optional: Add pom-pom or bow on top.

**Size chart:**

Note number of stitches to cast on for stockinette length.

**Full-term:** 66 stitches for 5 to 5.5 inches

**X-Large Preemie:** 58 stitches for 4 to 4.5 inches

**Medium Preemie:** 44 stitches for 3 to 3.5 inches

**Small Preemie:** 40 stitches for 2.5 to 3 inches

**X-Small Preemie:** 36 stitches for 2.5 inches

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**KNITTER POWER**

CONTINUED FROM PAGE 1

nization Partners in Health, Rosenberg has volunteered to coordinate a knit-a-cap campaign to save infant lives.

As the registered nurse specialist who developed and now helps manage NIH’s collaboration with the D.C. department of health to fight the District’s HIV/AIDS epidemic [the D.C. Partnership for HIV/AIDS Progress], Rosenberg is a “nurse navigator,” a title unique to this position.

Think about what it takes to deal with a single bureaucracy. Rosenberg tacks between a federal agency, a city health department, several hospitals and community clinics. Compared to this complexity, knitting sounds soothing.

It all started when her daughter, Naomi Rosenberg, sent her an email: “She said, ‘Mom, babies are dying of hypothermia in Rwanda. Ask some of your friends who knit if they can help.’

So far, Rosenberg has made, collected and shipped 280 caps since last October, and more are needed.

“They tell us to keep them coming,” she says.

One hundred babies per month are born at Rwinkwavu Hospital in Rwanda, the first Partners in Health-built hospital in Africa. It’s one of the sites where Naomi once worked as an assistant to Farmer, who co-founded PIH in 1987. She is now a medical student at the University of Pennsylvania.

Rwanda, in east-central Africa, is near the equator. Yet because it’s in a mountainous region, Rwanda gets cold. Premies are especially vulnerable, but even full-term babies need caps.

Still recovering from the 1994 genocide in which an estimated 800,000 people were killed, Rwanda is making progress: Its infant mortality rate is down to 112 per 1,000 live births. The U.S. rate is around 6 per 1,000 live births.

“They have only one incubator [in Rwinkwavu Hospital],” says Rosenberg. “They once had to put four babies in it together, head to toe…”

PIH works to bring modern medical care to poor communities in nine countries around the world. The President’s Emergency Plan for AIDS Relief was based on PIH’s groundbreaking model in Haiti. Now Rosenberg’s full-time job fighting HIV/AIDS in Washington, D.C., dovetails with her volunteer effort for PIH.

“I’m basically a public health nurse,” she said.

“When the World Trade Center went down, I got in my car and went to help.”

The cap project “takes almost no investment,” as Rosenberg puts it. “Anybody who knits has a plastic bag of scraps they’re saving for a project someday. I can make two of these hats while I’m watching the football game.”

Note to knitters: Use acrylic yarn, because it’s washable. Even if you don’t knit, you probably know somebody who does.

“Nurses at Rockledge and on the eighth floor of the CRC are contributing,” Rosenberg says. “And I’ve got my book club making caps.”

So this is a true-love story, even though the characters may never meet. It’s about babies born in poor, rugged surroundings in a recovering nation. It’s about a nurse with a plan to keep them from dying of cold, one by one, stitch by stitch. It’s about knitter power.

“The world is uneven,” Rosenberg says, “and this is one of the things I can do to help.”

Baby cap drop-off location is in Dr. Steven Rosenberg’s office, Bldg. 10-CRC/3-3940, or email Alice Rosenberg directly at arosenberg@mail.nih.gov.

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**NICHD, NCNW Note Successful Community Effort**

NIH and the National Council of Negro Women (NCNW) have developed “Fit for Life,” a community-based obesity prevention program for young people ages 11 to 13. The project includes a workshop for adults and caregivers and one for young people, to help children maintain a healthy weight through improved food choices, increased physical activity and reduced screen time. The program is being carried out through NCNW’s network of regional leaders around the country, who are presenting the workshops to parents and young people in their communities and training other NCNW members to do the same.

Leaders from both organizations recently held a plenary session during NCNW’s 54th National Convention at National Harbor, Md., to highlight the efforts and success of NCNW regional leaders in bringing these materials into their communities. Shown in the foreground are Dr. Dorothy Height (l), NCNW president emerita and Dr. Yvonne Maddox (r), NICHD deputy director.
SIDS Linked to Low Levels of Serotonin

The brains of infants who die of sudden infant death syndrome (SIDS) produce low levels of serotonin, a brain chemical that conveys messages between cells and plays a vital role in regulating breathing, heart rate and sleep, reported researchers funded by NIH.

SIDS is the death of an infant before his or her first birthday that cannot be explained after a complete autopsy, an investigation of the scene and circumstances of the death and a review of the medical history of the infant and of his or her family. According to the National Center for Health Statistics, SIDS is the third leading cause of infant death, claiming more than 2,300 lives in 2006.

The researchers theorize that this newly discovered serotonin abnormality may reduce infants’ capacity to respond to breathing challenges, such as low oxygen levels or high levels of carbon dioxide. These high levels may result from re-breathing exhaled carbon dioxide that accumulates in bedding while sleeping face down. The findings appeared in the Feb. 3 issue of the Journal of the American Medical Association.

Antibodies Against Abnormal Glycoproteins Identified as Possible Biomarkers for Cancer

Scientists have found that cancer patients produce antibodies that target abnormal glycoproteins (proteins with sugar molecules attached) made by their tumors. The result of this work suggests that antitumor antibodies in the blood may provide a fruitful source of sensitive biomarkers for cancer detection. The study, supported in part by the National Cancer Institute, appeared in the Feb. 15 issue of Cancer Research.

“Thanks to emerging technologies such as the one used in this study, scientists have identified biomarkers based on the carbohydrate (sugar) portion of a glycoprotein that may be novel targets for early detection and diagnosis of certain cancers,” said Dr. Sudhir Srivastava, chief of the cancer biomarkers research group in NCI’s Division of Cancer Prevention.

Research has shown that cancer patients sometimes make autoantibodies against their own malignant cells and tissues, as part of an immune response against their cancers. It is unclear why some cancer cells evade immune defenses. Scientists hope that such antibodies may ultimately have the potential to help doctors detect cancer by a simple blood test.

Vaccine Protects Monkeys from Chikungunya Virus

An experimental vaccine developed using non-infectious virus-like particles (VLP) has protected macaques and mice against chikungunya virus, a mosquito-borne pathogen that has infected millions of people in Africa and Asia and causes debilitating pain, researchers at NIH have found.

Scientists at NIAID developed the vaccine because there is no vaccine or treatment for chikungunya virus infection. Details about the vaccine were published Jan. 28 in the online version of Nature Medicine.

“Increases in global travel and trade, and possibly climate change, may be contributing to the spread of disease-carrying mosquitoes into new areas,” said NIAID director Dr. Anthony Fauci. “Finding safe and effective human vaccines for chikungunya virus and other insect-borne pathogens is an important global health priority.”

“This virus-like particle vaccine provides a promising way to protect against an emerging infectious disease threat,” noted Dr. Gary Nabel, director of NIH’s Vaccine Research Center. “This same approach could possibly extend to viruses related to chikungunya that cause fatal diseases such as encephalitis.”

Teaching Teens About Abstinence May Delay Sexual Activity, Reduce Risk Behaviors

Teens who received a behavioral intervention centered on abstinence were more likely to delay first sexual contact than teens who received a control intervention focusing on general health promotion, according to an NIMH-funded study. Though differing from federally funded abstinence-only programs, the abstinence-based intervention may help delay sexual activity among adolescents. The work is described in the February 2010 issue of the Archives of Pediatrics and Adolescent Medicine.

Sexually active teens face a broad range of potentially negative outcomes related to HIV and other sexually transmitted infections and unplanned pregnancies. In particular, African-American teens experience these outcomes at much higher rates than their peers.

According to the researchers, their study shows that a theory-based, abstinence-only intervention may be an effective method for delaying sexual initiation in middle school students who are not already sexually active.
Snowfalls Beautify Campus

It wasn't the biggest snowfall of the season, but the Feb. 3 storm (shown in all images except bottom left) that brought close to 5 inches of wet snow to the campus was among the most beautiful. The flakes clung to each shoot and twig, giving the bare trees the glamour of cherry blossoms in full bloom. It won't be long until the real cherry blossoms open, and it's likely that many NIH'ers can't wait for that day, as twin major storms on Feb. 5-6 and Feb. 10-11 closed federal offices for almost a week. The photo below was captured by Zachary Dezman, a fellow in the NIH Clinical Research Training Program, who skied to work on Saturday, Feb. 6 and took the picture.

PHOTOS: LYDIA POLIMENI, VALERIE LAMBROS, ZACHARY DEZMAN