SAN DIEGO'S CHIEF EDUCATOR

Superintendent Cindy Marten talks about why she wants a new evaluation process for teachers and more flexibility in class sizes. **SD5**

SD IN DEPTH SUNDAY

Stem cell pioneer Jeanne Loring collaborates with a wide range of scientists and industry leaders to expand the field's influence

SPREADING THE GOSPEL

BRADLEY J. FIKES • U-T

Few medical advances equal stem cells in their promise to treat conditions that currently have no cure. From Parkinson's disease to AIDS to spinal-cord injuries, scientists are getting ever closer to realizing that promise for hundreds of millions of patients.

Yet when Jeanne Loring began her research pursuits in the late 1970s, few people knew what stem cells were. These microscopic wonders, with their ability to turn into many different types of cells in the body, fascinated her. She has devoted her career to studying them — and encouraging others to do likewise.

Loring, in short, is a stem-cell evangelist.

She commands respect worldwide — not only because she was one of the first people to become proficient

SEE **LORING • SD2**

The Scripps Research Institute's Jeanne Loring, shown at her Del Mar home, is a leader in the stem-cell field. K.C. ALFRED • U-T

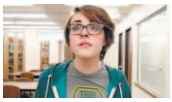
WINNERS & LOSERS

Your weekly news score card

WINNERS

DNA magic: A team led by scientists from the Scripps Research Institute in La Jolla expand the DNA genetic code, opening the door for new medical treatments and other life-changing advancements. "A" stands for "awesome."

Hot "Frozen": Point Loma Nazarene University student Olivia Mowry (above right) makes a "Frozen" parody video extolling the study-enhancing powers of Starbucks and YouTube adoration



follows. Make that Champagne toast a venti.

The big pop-in: President Barack Obama visits San Diego for a few whirlwind hours. Equal opportunity protesting, lobbying and lookiloo-ing ensues.

Global outrage: The U.S. provides manpower and resources to aid the worldwide campaign to find the hundreds of Nigerian girls kidnapped from their boarding school by a militant group last month.

Shopping! Affordably fabulous British clothing chain Topshop/Topman will make its San Diego debut at the Fashion Valley Mall in October. The line forms behind me.

LOSERS

Not the NFL Draft: Because nothing is as important as the NFL Draft. Nothing. Shouldn't you be watching it right now?

Global health: A new federal report says that global warming is already leaving its mark and our extreme weather will only get worse. Time to break out the asbestos galoshes.

Target: As the discount retailer struggles with the fallout of the Black Friday data breach, Target CEO Gregg Steinhafel (right) resigns after 35 years with the company.

Fire fears: Officials warn that California is facing its worst fire season ever. Check readyforwildfire.org and saveourH20.org for preparedness tips.

The VA: Embattled Veterans Affairs Secretary Eric Shinseki faces calls for his resignation while announcing a nationwide audit of access to VA care. The San Diego VA remains above the fray.

KARLA PETERSON • U-T

LORING

Scientist knew she wanted to work in a field with constant collaboration

Jeanne Loring holds a petri dish with pluripotent stem cells from a Parkinson's patient. HOWARD LIPIN • U-T

FROM SD1

in producing human embryonic stem cells in the lab, but also because her collaborative spirit has been foundational in expanding the stem-cell field to new generations of scientists.

At the request of the National Institutes of Health, she co-wrote a manual on the subject to train other researchers. She also provided knowledge that was crucial in courtroom battles against a patent that had put a stranglehold on stem cell studies nationwide. And she helped establish a trailblazing training program for stem-cell scientists in Southern California.

Today, as a leading figure at The Scripps Research Institute in La Jolla, Loring is widely considered both a stem-cell pioneer and a key voice on the latest issues in the field.

She's a board member of the institute that funds and coordinates much of the stem-cell research in California. She revels in teamwork with experts at other scholarly institutions, in industry and from patient-advocacy groups. And she's internationally renowned for her findings on how stem cells might treat neurological diseases.

But Loring is happy to be more of a behind-the-scenes player.

"Sometimes you hear about scientists who are pie-in-the-sky crazy people, and you've got to lasso them back down to Earth. That's not a problem with Jeanne. She's got her feet planted firmly on the Earth," said Daniel Ravicher, an attorney with the Santa Monica-based group Consumer Watchdog and founder of the Public Patent Foundation.

Loring said she values the dynamics of experts working together. It's a conspicuous contrast to the largely solitary career of her geologist father, who did much of his prospecting alone in the deserts of Western states.

"I could not see myself doing that," Loring said. "It was too lonely. The biological sciences require you to talk to people a lot."

Unlike the "pure" academic who regards partnerships with businesses as compromising science, Loring said ties with industry can be rewarding. Businesses can take basic research discoveries and turn them into drugs and other therapies, she said, and that "translational" arrangement is hard to replicate in a walled-off academic setting.

While working for biotechs in the San Francisco Bay Area relatively early in her career, Loring developed a patented mouse model of Alzheimer's disease and a patented method for determining the amount of plaque in brain cells taken from deceased Alzheimer's patients. She also helped a company test fetal brain cells as a potential therapy for Parkinson's disease; the technique failed because the technology was too primitive.

Loring's work now mainly concerns artificial embryonic stem cells, called induced pluripotent stem cells. Grown from skin, they don't raise the thorny ethical issues linked to embryonic stem cells and can be custom-made for individuals.

"Sometimes you hear about scientists who are pie-in-the-sky crazy people, and you've got to lasso them back down to Earth. That's not a problem with Jeanne. She's got her feet planted firmly on the Earth." Daniel Ravicher • attorney with Consumer Watchdog

Public duty

Loring frequently speaks out on issues concerning science. As the recipient of government grants, she said she has an obligation to keep the public informed and make the best use of taxpayer money.

In 2006, Loring joined a legal challenge to some patents held by the Wisconsin Alumni Research Foundation, or WARF, on deriving human embryonic stem cells. The patents unfairly prevented many scientists from engaging in the field, she said.

The litigation, led by the nonprofit Consumer Watchdog, has largely succeeded in reducing the patents' scope.

Loring provided scientific expertise deemed pivotal in rebutting WARF's assertions, said attorney Ravicher. For example, she undermined the foundation's legal claim that its derivation method wasn't "obvious."

The WARF patents covered a method of making human embryonic stem cells that was previously used on various animals. The foundation reasoned that applying the method to human embryos wasn't obvious because human embryos are different from animal embryos.

"(Loring) was the one who came up with the argument that while all these embryos are indeed different from human embryos, they're all different from each other as well," Ravicher said.

Over the years, Loring also has warned her stem-cell colleagues that they can lose the public's trust because of repeated examples of fraudulent or shoddy science.

Earlier this year, Japanese and American scientists published research on how to produce stem cells through simple methods such as dipping cells in an acid bath. The research was later found to contain grave errors that made it invalid.

Loring was interviewed by a Japanese journalist about the debacle surrounding these so-called "STAP" cells.

"He asked me, 'Could that happen in your lab?' I said no, because (our scientists) all work together. They'd have to conspire," she said. "The structure of the way you do science can encourage dishonesty, and you can discourage it by structuring it differently."

Not only for nerds

Loring was born in 1950 in Tucson, Ariz., to William and Elizabeth "Liz" Loring. She has a sister, Anne.

The family periodically moved across the far West as her father prospected for uranium with a Geiger counter in desert after desert. Loring credits him with providing an education that was impossible to get at the small towns where she went to school.

"My father was a real intellectual. He wrote poetry and he read all the classics, and he'd often read them to me," she said. "He expected my sister and I to be articulate. He expected us to appreciate literature. I almost felt like I was home-schooled. I went to schools where I knew more than the teachers did."

In 1967, Loring's unofficial education and her own studies paid

SEE LORING • SD8

Loring's latest pursuits

Jeanne Loring's current projects include:

• Eight San Diego-area Parkinson's patients are expected to receive an IPS cell treatment Loring helped develop. Brain cells grown from the patient's own IPS cells are to be transplanted into their brains next year, if federal regulators approve.

• In mouse models of multiple sclerosis, therapy with neural stem cells restored movement, something Loring wants to try in people. Surprisingly, the treated mice improved although the transplanted cells all died.

• Stem cells from endangered species such as the white rhino (above) have been created by Loring and her lab with the help of the San Diego Zoo. This frozen collection of cells may one day allow the resurrection of species verging on extinction or perhaps already extinct.

TREATMENTS REACHING PATIENTS

Hundreds of clinical trials using stem or regenerative cells are taking place in California and around the world

BRADLEY J. FIKES • U-T

After many years of waiting, a flood of new regenerative-cell therapies is finally reaching patients. Hundreds of clinical trials for these experimental treatments are under way across the world.

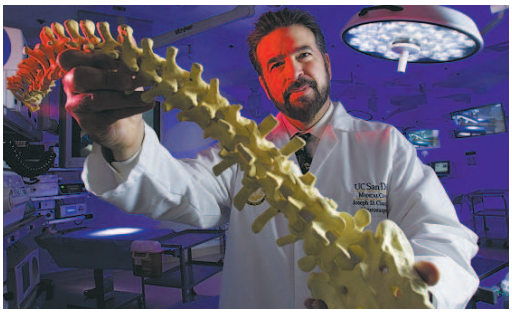
In the United States, 774 trials with stem or other regenerative cells are open to patients or soon will be, according to clinicaltrials.gov, which lists government-approved clinical testing in this country and abroad. Of that total, 147 are taking place in California.

One of the most difficult tests involving stem cells — repairing spinal-cord damage that has caused complete loss of movement and sensation below the injury site — is set to begin soon at UC San Diego.

Patients in that study will get injections of fetal-derived neural stem cells in and around the injury site, along with physical therapy and immune-system drugs in case there's a reaction to the stem cells. The trial will use a device that delivers precisely targeted "microinjections" of cells to the targeted areas.

The clinical trial will test safety and look for early signs of efficacy, said Dr. Joseph Ciacci, a UC San Diego neurosurgeon leading the testing.

A study published a year ago found that in rats with spinal-cord injuries, the neural stem cells significantly improved movement in the hind paws. Ciacci, who co-authored that study, saw the cells proliferate and fill in a spinal-cord cavity that had resulted from the injuries. Such results supported testing the therapy in people, he said, but he declined to say whether he expected to see any improvement in those patients.



UC San Diego neurosurgeon Dr. Joseph Ciacci will be leading a clinical trial involving stem cells to treat paralysis from spinal-cord injury. HOWARD LIPIN • U-T

"I really don't know, because it's not been done," Ciacci said.

The clinical trial is expected to start in June. It's intended for adults 18 to 65 years old who suffered their injury at least one year ago but no more than two years ago. For more information, visit utsandiego.com/ucsdspinal or call Amber Faulise at (858) 657-5175.

Another type of stem cells, mesenchymal stromal, might be described as the duct tape of regenerative cells. Generally derived from bone marrow, they are being tested for treatment of pulmonary fibrosis, multiple sclerosis, kidney transplants, liver cirrhosis, osteoarthritis of the knee, stroke and many other conditions. Worldwide, 226 trials are being conducted with these cells, including 45 in the U.S. and 12 in California, according to clinicaltrials.gov.

These cells function as "natural immune regulators," said Jacques Galipeau, a professor of hematology and medical oncology at the Winship Cancer Institute at Emory University in Atlanta. Galipeau is leading a study on using these cells to treat Crohn's disease, an inflammatory autoimmune disorder of the bowels. Information on his test can be found by searching for "Galipeau" at clinicaltrials.gov.

Mesenchymal stromal are babysitters for blood-forming stem cells, guiding their development, Galipeau said. They also act as traffic cops for immune-system cells and help in repairing injuries.

"Mesenchymal stromal cells seem to be able to mobilize from bone marrow and other tissues in which they nest — fat, for example — and participate in the repair response," Galipeau said. "And a big part of what they do is to regulate inflammation."

While Ciacci's trial uses stem cells taken from other people, Galipeau is using each patient's own mesenchymal cells that were multiplied in the laboratory and infused back into that person.

Nothing needs to be done to the cells — "no genetic engineering, nothing spooky," Galipeau said. "The natural property they possess is that they hose down inflammation."

The anti-inflammatory property of these cells makes them suitable for treating a wide range of immune diseases, Galipeau said.

Larry Goldstein, head of stem cell research at UC San Diego, said stem-cell treatments are reaching clinical trials "pretty speedily," considering how much basic research had to be done to get the technology ready.

"Brain injury, spinal-cord injury, neurodegenerative disease, drug development — it's really a terrific broad portfolio of things that are moving into the clinic," Goldstein said. "The thing that makes me most unhappy is, as a consumer, I desperately want everything to be ready to apply to patients successfully tomorrow, not in years. But we've got to do it by the book so that we don't hurt anybody, and we have to do it in a way that's efficacious.

"But I'm always frustrated at the rate of progress. If you have a sick family member or you yourself are sick, it's never fast enough."

bradley.fikes@utsandiego.com
(619) 293-1020
Twitter: @sandiegoscience

LORING • She has long been driven to apply knowledge to practical uses

FROM SD3

off when she won a National Merit Scholarship. The money allowed her to attend the University of Washington in Seattle, where she earned a bachelor's degree in molecular biology.

Loring had started out as an English major and added science classes as a secondary interest.

"I was good at science, but I thought it was only for nerds," Loring said.

She soon changed her mind. "I found I was doing a lot better in the science classes than I was in the literature classes, and I was enjoying them more."

Loring described herself as discreetly "ultra-competitive" during her university days. While working to land top grades on tests, she avoided calling attention to herself for fear of offending male egos.

"I got the highest score in my biochemistry class, and the professor announced that in class. I refused to go up there, because I didn't want anyone paying attention to me," she recalled. "I didn't want the pressure — 'Oh my God, a girl beat me.' I didn't want to evoke that."

Loring continued her schooling with graduate studies at the University of Oregon in Eugene, where she ran into trouble: Her adviser wanted her to work on her own, not collaborate with others.

"It seems absurd in retrospect, but his style was, 'You do your own project.' You could talk with other people but you couldn't work with them. He kept getting angry with me for that," Loring remembered.

In another development, Loring met her future husband, David Barker, at the same university. He was a professor there, and they were both married at the time.

"It was quite a scandal," she said.

(Barker's own career is notable; he was once the chief scientific officer for the DNA sequencing giant Illumina, which is headquartered in San Diego.)

Astronomy is among the interests Jeanne Loring pursues in her scant free time. The Scripps Research Institute researcher and her husband try to take an annual solar eclipse vacation. K.C. ALFRED • U-T

Loring eventually obtained a doctorate in developmental neurobiology at the University of Oregon. It was a direct precursor to her work with embryonic stem cells.

"I studied neural crest stem cells. There were no embryonic stem cells (known to scientists) then; those were not made (in the lab) until the early 1980s," she said. "My thesis was — in a very primitive way — how neural crest cells made the decision to be a neuron or pigment cell, and how I could influence them by culturing them differently. The concept of having a cell that could do multiple things interested me."

Academia and biotech

Loring began her professional career as a temporary assistant professor at UC Davis in 1982. She left five years later, concluding that she would never get a tenure-track position there. She was also eager to begin putting her research knowledge to more practical uses.

That opportunity came in 1987, when she was hired as a senior staff scientist at Hana Biologics in Alameda. Among its projects, the biotech company was developing a treatment for Parkinson's disease using cells grown from fetal brains.

"It's a completely different world than in academia," Loring said. "We're talking about clinical trials ... and I learned from them that it was possible to go from a lab experiment into a clinical trial."

But the envisioned treatment didn't work, and Hana Biologics went under.

Loring kept adding to her skills with each new job.

At the next workplace, GenPharm in the Bay Area, Loring designed the mouse model of Alzheimer's disease. She and colleagues became skilled at writing applications for federal grants, mainly for stem-cell research.

"It was the richest scientific environment I was ever in, and it was the most collaborative," Loring remembered.

GenPharm failed in 1995 after a lawsuit derailed plans for it to hold a public offering. Loring was more fortunate: She had four years left on a Small Business Innovation Grant for making rat embryonic stem cells, and it was transferable to another company.

"I learned that if you have your own money, you have lots more choices," Loring said.

Access battle

During the late 1990s, she decided it was time to move from rat embryonic stem cells to the human kind. She founded a company to do so — Arcos Biosciences in San Mateo.

Producing human embryonic stem cells was much more difficult because the embryos and government funding for such research were harder to obtain at the time.

It became even more difficult when the Wisconsin Alumni Research Foundation received patents for creating human embryonic stem cells. University of Wisconsin scientist Jamie Thomson became famous for isolating those long-elusive cells in 1998.

The WARF patents frightened off investors for various stem-cell ventures, Loring said, and Arcos folded.

By then, Loring had derived nine lines of human embryonic stem cells, which were among the lines President George W. Bush approved for federal funding in August 2001. They were subsequently acquired from Arcos by CyThera, a San Diego-based biotech firm.

That company, since renamed as ViaCyte, is preparing to start human clinical trials of a treatment for Type 1 diabetes, using insulin-producing cells derived from embryonic stem cells.

Loring moved to San Diego in 2003, when she returned to academia by joining the Sanford-Burnham Medical Research Institute. Evan Snyder, a prominent stem-cell scientist, jokingly said he saved Loring from the "dark side" — industry — by recruiting her.

Together, they launched what may have been the first stem-cell "core facility" in Southern California and the region's first training program for stem-cell researchers, Snyder said.

Even after Loring moved to The Scripps Research Institute in 2007, she maintained her professional endeavors with Snyder.

"We were always co-workers and collaborators," Snyder said. "In fact, she has an adjunct appointment at Sanford-Burnham. She stays completely involved, and I've stayed actively involved with the Scripps program."

Away from science

With so much to do, it's hard for Loring to find leisure time. There's always some task in the lab. And even when Loring travels, it's almost always work-related.

"I go to a conference probably every month," she said. "It's not a break from work, it's working someplace else. Part of our jobs is to tell people about our work, and you have to go somewhere to do it."

But Loring and her husband give themselves one respite a year: They take a solar eclipse vacation.

"The eclipse vacations are the perfect thing for us," Loring said. "You can always work, but the eclipse is going to happen at a certain time and a certain place, and you have to be there when it happens. Almost every year, there is an eclipse somewhere exotic — Bolivia, Zambia. We went to Libya."

A decade ago, when there was no solar eclipse to view, Loring and Barker took a vacation to Australia for another purpose: After many years together, they got married.

bradley.fikes@utsandiego.com
(619) 293-1020
Twitter: @sandiegoscience