tain to intensify interest in a separate lawsuit, in which environmentalists are attempting to block the U.S. Navy from deploying a new sonar that some researchers say could harm whales. Remarkably, the Mexican incident occurred on the same day that more than a dozen beaked whales stranded off the Canary Islands in the eastern Atlantic, following naval exercises conducted by U.S. and Spanish vessels. –DAVID MALAKOFF

ENDOCRINOLOGY

Divorcing Estrogen's Bright and Dark Sides

Despite concerns about the risks of hormone replacement therapy for postmenopausal women, one benefit has not been challenged: It makes bones stronger. Now a study on page 843 suggests that it might be possible to tease apart the various effects of estrogen, maintaining its benefits while reducing its risks. A synthetic hormone has been shown to boost bone strength in mice without affecting reproductive organs.

Estrogen makes women less likely to develop osteoporosis and suffer debilitating fractures. But this boon apparently comes with increased risk of breast cancer, pulmonary embolism, heart attack, and stroke (*Science*, 19 July, p. 325). Reasoning that estrogen's effects on various tissues might be mediated by different cell signaling cascades, a team led by Stavros Manolagas of the University of Arkansas for Medical Sciences in Little Rock has been identifying synthetic hormones that activate only a subset of these pathways.

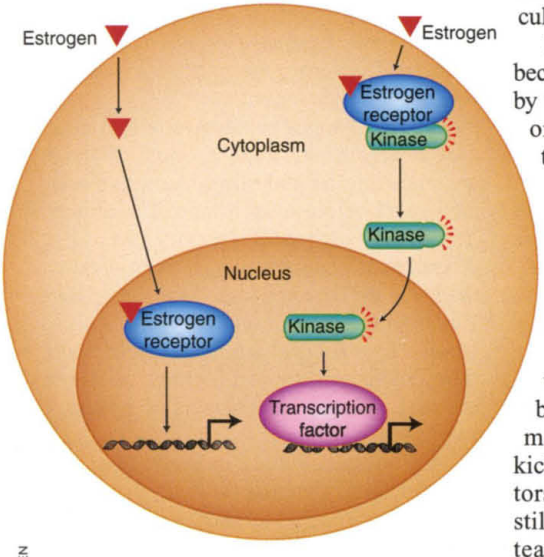

ILLUSTRATION: C. SLAYDEN

Choosing the right message. Synthetic hormones that bypass the traditional estrogen pathway (left) and activate the "nongenotropic" pathway (right) might prevent bone loss without side effects.

Whether such compounds will prove useful in humans remains to be seen, but other researchers and clinicians say the new study is a promising first step. "If it holds up, then it's quite important," says molecular endocrinologist Geoffrey Greene of the University of Chicago. "If compounds like estrogen could be used to maintain bone density with few or no side effects in aging women, that would be huge."

The researchers gave a compound named estren to adult female mice whose ovaries had been removed. As with menopause, ovariectomy curtails estrogen production and eventually leads to a decline in bone density. Estren reversed this change and restored bone strength as effectively as—and in some cases more effectively than—estrogen.

Estren apparently strengthens bones by tinkering with the cellular construction crews that constantly remodel them. At any given time, Manolagas says, there are 5 million to 10 million sites on a human skeleton where cells called osteoclasts dig tiny trenches in the bone that are filled in by bone-forming osteoblasts. After menopause, osteoclasts outpace osteoblasts, making bone more porous and brittle. Manolagas's team found that estren (as well as estrogen) tips the balance in the other direction: Both compounds encourage osteoclasts to self-destruct while prolonging the life of osteoblasts.

Despite their similar effects on bone, estren and estrogen have markedly different effects on the reproductive organs, the team found. In ovariectomized mice, the uterus loses nearly two-thirds of its weight. Estrogen, but not estren, prevents this loss. And whereas estrogen stimulated the growth of cultured breast cancer cells, estren did not.

Manolagas says these differences arise because estren doesn't activate the pathway by which estrogen acts on the reproductive organs. In that pathway—traditionally thought to be the only means for estrogen signaling—the hormone diffuses into the nuclei of cells, where it binds to its receptor and a complex of other proteins that together regulate the transcription of certain genes.

Recently, Manolagas and others have suggested that estrogen can activate a "nongenotropic" pathway, whereby estrogen alters gene expression by means of a biochemical cascade that kicks off when the hormone binds receptors outside the nucleus—an idea that is still controversial. Last year Manolagas's team reported that estrogen's effects on osteoblasts and osteoclasts seem to be mediated by this pathway. The new study suggests that estren activates this pathway but not the traditional one, which would explain its preferential effect on bone.

ScienceScope

Kid Drug Rule Blocked An effort to force companies to test new medications in children has suffered a setback. A federal court in Washington, D.C., last week struck down a 1998 Food and Drug Administration (FDA) rule aimed at developing safe dosing regimens for children. But supporters of the pediatric rule are urging Congress to override the court's order.

The pediatric rule required companies to include children in drug trials before FDA would approve any product likely to be prescribed for children. Prior to the rule, doctors complained that without tests, they had to guess how their small charges would respond to a particular drug. But FDA's move sparked a lawsuit 2 years ago from the Association of American Physicians and Surgeons and two other groups. They argued that Congress hadn't given the agency the power to mandate pediatric testing, and a federal judge agreed. Now, the American Academy of Pediatrics and other organizations are pushing Congress to formally give FDA that power. A vote on the issue could come as early as next month.

Spain's Stem Cell Standoff One of Spain's state governments is hoping to drill a loophole in the nation's restrictive policy on human embryo research. Officials in Andalusia last week announced that they plan a $2 million research center in Seville that will extract human stem cells from embryos that have been frozen for more than 5 years.

The center—to open next year and be led by Bernat Soria of Miguel Hernández University in Alicante—aims to sidestep a 1988 ban on research involving "viable" embryos. Since that vaguely worded law also forbids implanting embryos that are more than 5 years old, Andalusian officials argue that such embryos are not viable and therefore are accessible to researchers.

It's not clear if federal officials will agree. Health minister Ana Pastor, who has criticized stem cell research advocates, has called a "technical meeting" with Soria later this month. If she tries to scuttle the center, Andalusian officials could appeal to Spain's high court, notes geneticist Josep Egozcue of the Autonomous University of Barcelona. But public pressure to approve the center will be enormous, he predicts, noting that patient groups recently collected 1.3 million signatures on a petition calling for the government to back stem cell studies.

Contributors: David Malakoff, Jeffrey Mervis, Jennifer Couzin, Xavier Bosch

(No one is sure which pathway might be responsible for estrogen's apparent link to heart disease.)

The study, says Greene, supports the existence of nongenotropic pathways. Whereas most evidence has come from experiments with cultured cells, he says, the new study is "one of the most striking demonstrations" of such effects in live animals.

Many osteoporosis drugs are in the pipeline, but none boasts estrogen's track record for preserving bone, says Susan Ott of the University of Washington, Seattle. Time will tell if estren can bring out the best of estrogen therapy and leave its dark side behind. **–GREG MILLER**

PALEONTOLOGY

Cuts at Dino Monument Anger Researchers

Vertebrate paleontologists are up in arms about a plan to cut back on research at Dinosaur National Monument. Although monument officials say the move will benefit paleontology in the long run, some scientists charge that the plan is misguided. "This is a big step backward," says Kenneth Carpenter of the Denver Museum of Natural History in Colorado.

The monument, which straddles the border between Utah and Colorado, includes a dramatic quarry face and 853 square kilometers of fossil-rich backcountry. It is well staffed for a site run by the U.S. National Park Service, boasting a paleontologist, a preparator, and a curator.

Chipping away. Paleontologists are concerned that cuts at Dinosaur National Monument will hurt research.

Last year, monument officials were charged with drawing up a 5-year plan that would eliminate nine positions out of 50. In the new plan, announced earlier this month, the preparator and paleontologist positions will be combined into a "physical sciences resource manager." Research will be less than half-time. The monument's chief of administration and acting supervisor, Susan Richardson, says that the change will ultimately boost the monument's paleontology program, because the new manager will focus on attracting scientists, students, and funding there and on coordinating volunteers. "I think we're going to be able to make it way larger," she says.

But paleontologists say that using volunteers to prepare unique fossils is risky. What's more, the long training process and high turnover could make a volunteer program an "enormous waste of time," Carpenter says. He also doubts whether many paleontologists would have time to prospect for fossils in an area that's new to them.

Amy Henrici of the Carnegie Museum of Natural History in Pittsburgh, Pennsylvania, studies some of the oldest frog fossils in North America—which monument paleontologist Dan Chure found and has lent her. "It's very important for me to have them out there looking for more fossils," she says. The planned changes raise the prospect that her research, and that at the monument, would slow or halt, she says.

But Greg McDonald, who coordinates paleontological research for the National Park Service, says that each superintendent must decide how to meet the needs of his or her park. "There's the ideal," McDonald says, "and then there's the practical."

–ERIK STOKSTAD

EUROPEAN RESEARCH

Directive Could Give Postdocs Permanency

CAMBRIDGE, U.K.—Richard A'Brook has worked for more than a decade at the University of Dundee in Scotland—a steady job, you would think, but the epidemiological statistician is himself a statistic. He's one of a legion of contract researchers whose job security depends on their employers' fundraising prowess. Now, however, a new directive from the European Commission (EC) could lead to radical changes in how contract researchers, mainly postdocs, are employed, particularly in the United Kingdom and Ireland. It's a "right to equal treatment," A'Brook says.

The EC's Directive on Fixed-Term Work, incorporated into U.K. law earlier this month, mandates that E.U. nations "prevent the abuse of fixed-term contracts through their continuous use." Precisely how the rule is implemented is up to each country, explains the EC's Andrew Fielding, because "the situation on the ground is so different" from one country to the next.

In the United Kingdom, universities and other employers will be forced to give permanent positions to any research staff members whose positions are renewed and run longer than 4 years, unless they can offer good reasons for not doing so. The directive also requires that workers on fixed-term contracts be given "equal treatment" in terms of benefits such as paid holidays, maternity leave, and representation on departmental committees. Most E.U. nations already have rules protecting contract workers, but the directive is causing a considerable stir in the British Isles, where such regulation has been lacking until now.

According to the U.K.'s Association of University Teachers (AUT), some 59,000 academics are now on fixed-term contracts in the United Kingdom. And few of these researchers are bright-eyed trainees happy to live with uncertainty and low status: An AUT study showed that the proportion of research-only fixed-term contract staff members in the United Kingdom aged 30 or higher rose from 53% in 1995 to 63% in 2001. But because the clock started ticking on the new rules only this summer, they'll have to wait until July 2006 to see whether their status will change.

Larger, research-intensive campuses and institutions are not anticipating making wholesale changes. "This is really just enshrining in legislation good employment practice," says a spokesperson for the University of Cambridge, one of the country's biggest employers of contract research staff. Similarly, institutes run by Cancer Research UK will continue to employ postdoctoral researchers on fixed-term contracts as part of the charity's philosophy of regularly bringing in new blood and ensuring that postdocs move on for career development.

But the changes could have profound effects at smaller institutions, some of which are choosing to make life-changing decisions well before crunch time. The attitude at Robert Gordon University (RGU) in Aberdeen is "let's just get on with it rather than wait for others to force us to do it," says RGU's human resources director, Robert Briggs. Last August, the Scottish university moved its entire contract research staff onto the same open-ended contracts as the rest of its academic staff.

A'Brook anticipates a groundswell of support for RGU's approach. Real change, he says, "will depend on local unions or staff representatives actually pushing institutions to implement these things." **–KIRSTIE URQUHART**

Kirstie Urquhart is European editor for *Science*'s Next Wave, where a longer version of this article appears (intl-nextwave.sciencemag.org/cgi/content/full/2002/10/22/1).

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