Koski was recruited by then–Department of Health and Human Services (HHS) Secretary Donna Shalala to lead the newly promoted Office for Human Research Protections (OHRP) after a death in a gene-therapy trial brought increased scrutiny of patient safety in research. Once there, he worked to persuade institutions that protecting patients required obeying their "consciences" as well as federal rules. Since Koski's arrival, OHRP has begun developing a system in which institutions—rather than the government—grade themselves on their oversight programs. A report earlier this month from the Institute of Medicine supports this approach, as well as voluntary accreditation of human-subjects protection programs.

Bioethicist Mary Faith Marshall of the University of Kansas Medical Center in Kansas City says Koski was a "tireless ambassador" in campaigning for "shared goals." David Korn of the Association of American Medical Colleges (AAMC) in Washington, D.C., agrees that Koski "deserves a lot of credit" for promoting the idea that protecting human subjects should involve the entire institution. But Korn is still waiting to see if the office follows AAMC's advice on the issue of reducing financial conflicts of interest. Koski says he hopes final guidelines will be out by the end of the year.

Some patient advocates and members of Congress, however, are pushing for mandatory standards. And one government official is skeptical that Koski accomplished much with OHRP's more than doubled budget and staff. "His brief tenure was reminiscent of a placebo: Some people thought it worked," quipped the official.

Koski insists that his departure "is not a political decision" but rather marks the end of a 2-year leave from Harvard in Massachusetts, where his family still lives. However, his time at HHS was not always smooth sailing. Koski often failed to follow proper procedures for developing policies and releasing information, one official says.

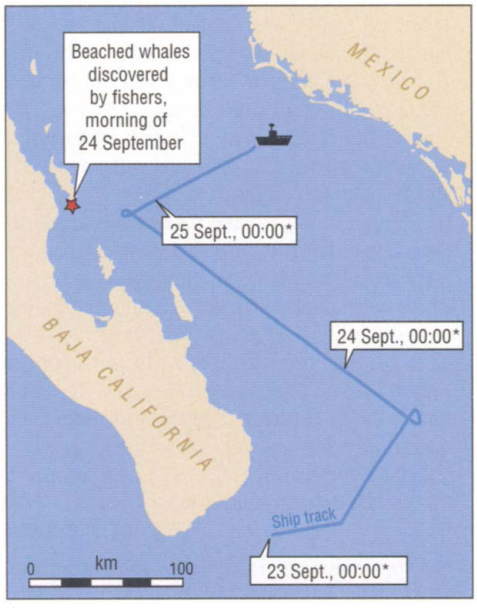
The office was also caught up in a revamping of HHS advisory committees (see p. 732). Koski acknowledges that he did not expect HHS's decision to let lapse the charter of OHRP's advisory panel, which Marshall, the chair, says "shocked and dismayed" members. HHS now plans to convene a smaller group, with 11 members instead of 17, and has revised its charter to include specific topics, such as protection of fetuses and embryos, that reflect the Bush Administration's opposition to abortion. Fetuses are already mentioned in federal regulations for protecting human subjects, but Koski says including embryos is "a change." Korn says AAMC is "very concerned" about the membership of the panel: "I just hope it isn't packed with ideologues." –JOCELYN KAISER

SEISMOLOGY

Suit Ties Whale Deaths To Research Cruise

The U.S. National Science Foundation (NSF) has a whale of a problem involving sounds, lawsuits, and the high seas.

Last week an environmental group asked a federal judge to suspend an NSF-funded sea-floor mapping expedition off Mexico that it claims led to the deaths of two whales. NSF rejects a link between the deaths and the air guns used by shipboard researchers to generate sound waves, adding that the researchers were following the law.



* All ship track times are GMT. To correct to local time, subtract 7 hours.

Too close for comfort? The research vessel *Maurice Ewing* sailed near the island in the Gulf of California where beaked whales beached.

But the incident has curtailed an expensive international mapping project and reignited controversy over the impact of noise on marine mammals. The case, filed 17 October in San Francisco, California, by the Idyllwild-based Center for Biological Diversity (CBD), could also lead to new regulation of U.S. researchers who use sound at sea.

The controversy began 25 September, when five vacationing marine biologists sailing in Mexico's Gulf of California happened upon two freshly beached Cuvier's beaked whales (*Ziphius cavirostris*). The group, which included several beaked-whale experts, tried to inform Mexican colleagues about the unusual find. In the process, they discovered that the *Maurice Ewing*, a research vessel owned by Columbia University's Lamont-Doherty Earth Observatory in Palisades, New York, was conducting a seismic survey nearby. The ship was bouncing sound pulses produced by blasts of compressed air off the gulf's floor to map the margins of the continental plate.

Human-created noise, including the use of sonar by military vessels, has been linked to other strandings of beaked whales, a poorly understood group of species (*Science*, 26 January 2001, p. 576). Although there is still no clear explanation of how sound might harm the whales, the gulf strandings "just seemed too coincidental, given the history," says Barbara Taylor, one of the vacationers and a whale researcher at the government's Southwest Fisheries Science Center in La Jolla, California.

Five days after the incident, Lamont officials temporarily halted the $1.6 million, 6-week cruise to review environmental precautions. Lamont's director, Michael Purdy, says there is no clear link between the mapping and the strandings, noting that the *Ewing* appears to have been at least 50 kilometers from the animals when they stranded. But cruise managers ultimately decided to reduce noise levels, drop half the planned routes, increase efforts to spot and avoid whales, and end night work, when whale monitoring is impossible. Lamont is also paying for aerial surveys to look for new strandings and helping outside researchers study the noise signature produced by the *Ewing*'s air-gun array. The cruise is scheduled to end 4 November.

The additional precautions, however, don't satisfy some whale experts. Air-gun signals can travel 10 or more kilometers from the ship, they note, a distance far beyond the gaze of sentries. Beaked whales are notoriously difficult to spot, they add, moving quickly and staying submerged for 30 minutes or more. "The *Ewing* should cease operations; they don't have a workable plan," says John Hildebrand, a whale and acoustics specialist at the Scripps Institution of Oceanography in La Jolla.

The incident has also raised the complicated legal question of whether the researchers had the proper permits. Last April, Hildebrand asked the U.S. Marine Mammal Commission, a government advisory body, to review the planned cruise after becoming concerned about surveying in an area known to be rich in beaked whales. Lamont and NSF officials, however, concluded that the cruise did not need U.S. marine mammal permits as it would occur in Mexican waters, and the Mexican government approved the mission. The biodiversity center contests that interpretation of U.S. law, saying that cruise planners should have consulted with U.S. regulators.

As *Science* went to press, the judge was still deciding whether to halt the cruise. Even if it continues, CBD attorney Brendan Cummings hopes that the case will clarify which laws apply to U.S. research vessels. It is cer-

SOURCE: LDEO

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.

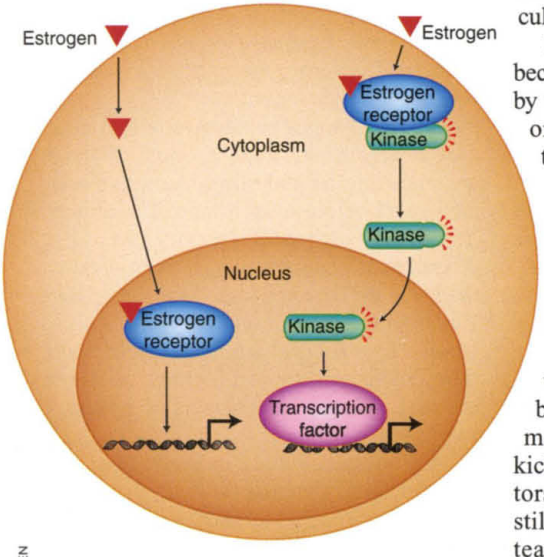


ILLUSTRATION: C. SLAYDEN

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.

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