Antitumor gene finds long-lost sibling

In the search for causes of cancer, gene sleuths have identified a new suspect: rogue *p73*. The normal version of this gene possesses the tools of *p53*—long known to have a criminal bent—and mimics some of its behavior. Moreover, investigators have placed *p73* at the scene of the crime—a part of the human chromosome previously implicated in tumor development.

The case is circumstantial so far, but researchers are hot on the suspect's trail, trying to pin down its activities.

The protein encoded by *p53*, when it functions normally, ensures that unhealthy cells won't reproduce. When the gene contains a defect, however, it allows cells to grow uncontrollably, leading to many types of cancer.

The importance of *p53* motivated many scientists to search for similar genes, but in vain. The discovery of *p73*, the first known relative of *p53*, thus came as a surprise. Daniel Caput at Sanofi Recherche in Labege, France, stumbled upon *p73* by accident, but he quickly realized its significance. He called Frank D. McKeon of Harvard Medical School in Boston, and a collaboration began.

"Daniel knew a good thing when he saw it," says McKeon. Caput, McKeon, and their colleagues describe the gene in the Aug. 22 CELL.

"The new finding is intriguing and may explain some previously mysterious aspects of *p53* biology," says Bert Vogelstein of Johns Hopkins Medical Institutions in Baltimore. For example, mice engineered to lack *p53* nevertheless develop properly, a perplexing result since the gene plays such a critical role in the health of cells. "A protein that can substitute for the p53 protein in some ways would explain this observation," says Vogelstein.

The p73 protein shows enough structural similarity to the p53 protein to support that speculation. The researchers found regions of p73 closely matching those that help p53 molecules stick to each other, and they showed that p73 can cling to p53 as well as to itself. The p53 proteins must adhere to each other in order to carry out their activities, such as turning on certain genes. In addition, p73 possesses stretches of amino acids like the ones that allow p53 to bind to DNA and activate genes, and p73 can turn on at least one of the genes that p53 targets.

Evidence implicating the *p73* gene mounted further when the researchers found that it resides near the end of human chromosome 1. Scientists have been eyeing this region for years because cells from several types of cancers lack pieces of DNA from this area. About 40 to 50 percent of neuroblastomas—the second most common solid tumor in children—contain such deletions, says McKeon.

Although one copy of chromosome 1 is missing some DNA in these cases, the other remains intact. Scientists have wondered why genes from the second copy can't cover for the missing ones. Caput, McKeon, and their team have now shown that ordinarily, one copy of *p73* does not function: Healthy people who have two normal, but slightly different, versions of *p73* use only one. If a cell loses the working gene, the other remains inactive.

Researchers must conduct additional experiments to establish the extent to which loss of the *p73* gene contributes to tumor development, says McKeon. "In that chunk [of chromosome 1], there's a lot of DNA and a large number of genes," he says. "*P73* could be just an innocent bystander." —*E. Strauss*

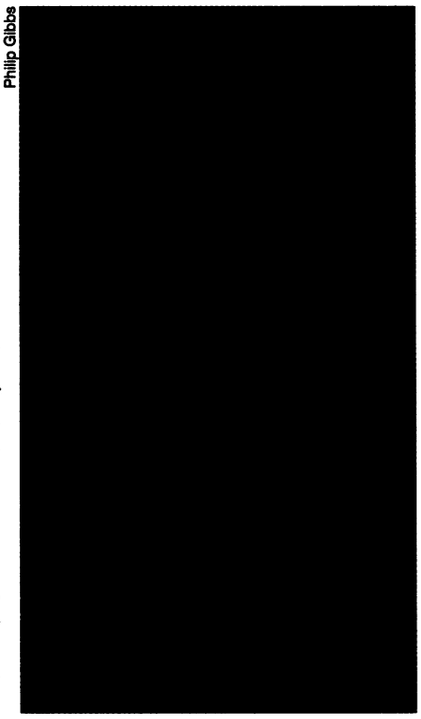
Endangered seals suffer massive die-off

Since May, a catastrophic epidemic has stricken the largest social group of Mediterranean monk seals, one of which is seen cavorting here. Of 270 seals living in a pair of caves on West Africa's Mauritanian coast, only about 70 have survived the disease, Albert Osterhaus told SCIENCE NEWS. A virologist at Erasmus University in Rotterdam, the Netherlands, Osterhaus heads an international group investigating the die-off. In the Aug. 28 NATURE, the team reports that most of the seals they examined harbor a dolphin morbillivirus, a virus similar to the one that causes distemper in dogs.

Osterhaus linked an earlier die-off of Baltic seals, caused by a related morbillivirus, to immunity-suppressing organochlorine pollution (SN: 7/2/94, p. 8). In the monk seals, however, he found no signs of a predisposing factor.

Only about 600 Mediterranean monk seals remain in the wild, mostly in groups of about 20. Osterhaus hopes that if many of them are inoculated with a distemper vaccine developed for their Baltic kin, they will weather this threat to their survival. —J. Raloff

Philip Gibbs



Mammograms better when timed to cycles

Women should get mammograms during the first 2 weeks of their menstrual cycle to avoid false-negative results, a Canadian study suggests.

Researchers at the University of Toronto assessed the accuracy of breast X rays on 6,989 women between the ages of 40 and 44 who had used oral contraceptives or estrogen in some form during their lives. The women provided information on their monthly cycle, with the first day of the menstrual period marking the start. The women then underwent mammograms, followed by breast examinations.

Among women tested during the last 2 weeks of their cycle, researchers found 24 cases in which the mammogram failed to detect tumors subsequently diagnosed as cancerous. Among women tested during the first 2 weeks of their cycle, researchers found only 15 such false negatives, even though screenings falling within the first 2 weeks slightly outnumbered those in the last 2 weeks. Tumors correctly detected by a mammogram were evenly split between the two time frames, the researchers report in the Aug. 15 CANCER. The number of instances in which the mammogram incorrectly indicated tumors was also similar between the two groups.

"Although I never like recommending changed behavior on the basis of one study, I can't see that women would be hurt by getting a mammogram in their first 2 weeks," says lead author Cornelia J. Baines, a physician and epidemiologist. Premenopausal women should get a breast examination whenever they get a mammogram, she adds. —*N. Seppa*