Cancer linked to aging DNA repair ability

Despite decades of progress in learning how chemicals, sunlight, and other environmental factors can increase one's risk of developing cancer, the reasons that some people develop tumors and others do not remain mysterious.

Now, researchers studying people with skin cancer have found new evidence that individuals differ not just in their susceptibility to these factors, but also in their ability to fix damaged genes. In addition, adults lose about 1 percent of their capacity to repair DNA each year, says Lawrence Grossman, a molecular biologist at Johns Hopkins University in Baltimore.

This loss may help explain why aging is a risk factor for cancer, adds Qingyi Wei, a molecular epidemiologist at Johns Hopkins.

Wei, Grossman, and their colleagues studied 88 people with basal cell carcinoma, an easily observed and readily treated cancer. The researchers also looked at DNA repair in 135 individuals with mild skin problems but not skin cancer. All study participants were Caucasians between the ages of 20 and 60. Researchers took blood samples and medical histories from them and asked questions about the number of severe sunburns they had had and the incidence of cancer in their families. Dermatologists evaluated the participants' skin condition.

The researchers then take an unusual approach to assessing an individual's ability to fix broken genes, Grossman says. They inject a small piece of genetic material into white blood cells extracted from each participant. The genetic material contains a mutant bacterial gene that normally codes for an enzyme the white blood cells never make. If the cells fix the gene, the gene then causes the cells to produce the enzyme. Forty hours later, the researchers measure the activity of that enzyme, which signals how well the cells have mended the gene.

The study revealed that young people with this skin cancer had the repair capacity of someone 30 years older. They also tended to have relatives with the disease. "This gives a clue that DNA repair capacity might be genetically linked," says Wei.

Overall, people with low repair capacity were five times more likely to develop the skin cancer if exposed to intense sun than those who had high repair abilities and stayed out of the sun. Also, women seemed more susceptible than men, especially if they had six or more severe sunburns, the researchers reported in the Feb. 15 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

As one of the first studies to combine laboratory and epidemiological data, "it verifies that effective DNA repair reduces the risk of cancer and that the magnitude [of that reduction] can be quite large," comments Richard Setlow of Brookhaven National Laboratory in Upton, N.Y.

Because of the body's gradual decline in repair capabilities, the researchers observed little difference in DNA repair capacities of older people. In them, differences in exposure to sunlight seemed critical to determining who developed tumors. "All that damage overcomes the repair system," says Wei.

"I think what people are starting to understand is that the link between aging and cancer is very, very close," says Grossman. "As you get older, you accumulate more and more persistent damage." He and his colleagues are now studying DNA repair in people with other types of cancer.

"It's an important paper that demonstrates that DNA repair plays a role in aging, which wasn't really demonstrated before," comments Vilhelm Bohr at the National Institute on Aging's Gerontology Research Center in Baltimore.

In addition, the differences between men and women suggest that hormones may influence DNA repair capacity. Grossman notes that, of the female participants, postmenopausal women who were receiving estrogen treatments retained 25 to 30 percent more repair capacity than other women their age. *— E. Pennisi*

Slow-motion slip may drive tsunami surprise

Because sudden jarring of the ocean floor or underwater landslides can trigger devastating waves, or tsunamis, people in earthquake-prone coastal regions have learned to run for high ground when the Earth begins to shake violently. Unfortunately, many people living on Nicaragua's Pacific coast barely felt the effects of a September 1992 earthquake. But just about 45 minutes after the main shock, say survivors, a tsunami reaching 10 meters high crashed onto a 300-kilometer-long stretch of the coastline.

More than 20 years ago, seismologist Hiroo Kanamori coined the term "tsunami earthquake" to describe such deceptively mild quakes that seem to spawn disproportionately large waves. Kanamori also proposed a possible explanation for the phenomenon, but the technical limitations of 1970s seismometers denied him compelling proof.

Now, based on seismic measurements taken during the Nicaraguan earthquake — the first event of its kind monitored with sensitive modern instruments — Kanamori and colleague Masayuki Kikuchi offer the clearest evidence to date that tsunami earthquakes stem from a "slow-slip" motion between oceanic plates. The seismic waves from this relatively gradual movement of the seafloor may scarcely be noticed by people on land.

Kanamori, of the California Institute of Technology in Pasadena, and Kikuchi, of Yokohama City University in Japan, report their findings in the Feb. 25 NATURE.

Judging from the seismic record of the Nicaraguan disaster, the researchers believe that the motion of oceanic plates in a deep trench off the Nicaraguan coast jiggled a 100-kilometer-long section of the ocean floor, moving it about 1 meter in a period of 2 minutes. The water set in motion by this event caused the surprise tsunami that destroyed 13,000 dwellings and killed more than 150 people.

Kanamori believes this slow slip — an event that releases great energy, but in a way that can mask its true magnitude — may prove the hallmark of the tsunami earthquake. During a slow-slip earthquake, he suggests, an oceanic plate lubricated by soft ocean sediments slides under an adjoining plate relatively slowly. This produces a seismic spectrum rich in long-period waves, like a piece of music full of cellos and bass drums. Seismic readings show clearly that long-period waves dominated the Nicaraguan earthquake, the researchers report.

Unfortunately, humans are only sensitive to the electric-guitar thrash at the higher end of the seismic spectrum — the kind of short-period seismic waves that shake buildings to their foundations. Thus, during a tsunami earthquake, people on land fail to notice the malevolent bass drone of impending inundation.

Until recently, seismometers were largely insensitive to long-period waves, a technical problem solved in the early 1980s. However, calculations of earthquake magnitude — the famous Richter scale — are still based on relatively short-period waves and thus may underestimate the destructive potential of tsunami earthquakes, Kanamori says.

Based on short-period waves, the Nicaraguan quake comes out as a magnitude 7.0 event. However, by using long-period waves to calculate the earthquake's "seismic moment," a quantity that reflects the actual motion of the plates rather than their ground-level effects, the researchers peg the Nicaraguan earthquake at a significantly larger magnitude 7.6.

Kanamori and others argue that use of long-period waves to calculate seismic moment, a task made quick and easy by modern technology, can provide an accurate determination of an earthquake's tsunami potential and perhaps offer sufficient warning to coastal communities at risk. Without such warning, the chances of surviving a tsunami traveling at freeway speed remain slim. "Once you see a tsunami coming towards you, it's usually too late," Kanamori notes. *— D. Pendick*