Biomedicine

Nighttime hormone helps starve cancers

Linoleic acid, the primary fat in corn oil, can fuel the growth of cancers in animals, a new study finds. However, a second study shows that tumors feed on this fat only in the absence of melatonin, a brain hormone produced at night. Together, these findings hold out the prospect of one day short-circuiting the growth of certain tumors with melatonin supplements.

In experiments, diets high in corn oil can leave an animal especially vulnerable to chemically induced cancers (SN: 6/24/89, p. 390). A report in the Sept. 15 CANCER RESEARCH now offers one possible explanation why.

Leonard A. Sauer and his colleagues at the Bassett Research Institute in Cooperstown, N.Y., implanted a liver cancer into the groin of rats. They encapsulated each tumor in a degradable wrap, leaving one blood vessel to feed the tissue and one to drain it. The researchers then fed the animals a diet in which the fat was mainly corn oil.

By tapping into the animals' blood as it entered and left the tumor, the researchers showed that the cancers altered the incoming linoleic acid into a chemical known as 13-HODE. In rats treated with a drug to prevent this transformation, linoleic acid exited the tumors unchanged. Moreover, these tumors grew far more slowly than those making 13-HODE did.

This fits with research by others showing that 13-HODE stimulates cell proliferation, notes David E. Blask, one of the authors.

In a second report in the same journal, Blask's group focuses on the role of melatonin, the brain hormone best known for its role in setting the body's biological clock. During the nighttime hours when an animal produced melatonin, tumor production of 13-HODE waned to negligible amounts. Cancers in these rats grew at roughly half the rate of those in rats with their melatonin-producing pineal gland surgically removed.

A third group of animals received extra melatonin. Late-afternoon supplements further slowed the growth of an implanted tumor, but early daytime melatonin had no effect. These data confirm something Blask had seen earlier—varying sensitivity to melatonin's cancer-inhibiting effect during daylight hours or nighttime illumination (SN: 10/17/98, p. 248).

Though the Bassett scientists did most of their work with liver cancer, they saw similar trends in 13-HODE's stimulation of two other cancers—and melatonin's inhibition of them. Concludes Blask, "This appears to be a generalized phenomenon." —*J.R.*

Cancers pick up GLUT of vitamin C

Leukemia cells, prostate tumors, and breast cancers are among malignancies that like to stock up on copious amounts of ascorbate, also known as vitamin C, a new study finds.

"We presume cancers do this because it gives them some advantage," speculates one of the authors, David W. Golde of Memorial Sloan-Kettering Cancer Center in New York City.

Earlier test-tube studies by Golde's team showed that tumor cells can't take up ascorbate. At a loss to reconcile this with data by others showing vitamin C in tumors, the Sloan-Kettering scientists implanted mice with human cancers and then probed the role of the host in the tumor's vitamin uptake.

In the Sept. 15 CANCER RESEARCH, they report that nearby stromal cells help the tumors by oxidizing vitamin C. In its new form, this material readily enters cancer cells' glucose transporters, or GLUTs. Golde notes that tumor cells have unusually high numbers of these pores, which normally regulate sugar's entry. Once inside a cancer cell, the oxidized material converts back to normal ascorbate, the new data show.

Radiation and many chemotherapy drugs kill cancers through oxidative mechanisms. Because ascorbate is a powerful antioxidant, Golde worries "that vitamin C [supplementation] might make cancer treatment less effective." —*J.R.*

Mathematics

Curving beyond Fermat's last theorem

When Andrew Wiles of Princeton University proved Fermat's last theorem several years ago, he relied on recently discovered links between Pierre de Fermat's centuries-old conjecture concerning whole numbers and the theory of so-called elliptic curves (SN: 11/5/94, p. 295). Establishing the validity of Fermat's last theorem involved proving aspects of the Taniyama-Shimura conjecture, which focuses on properties of elliptic equations. Now, four mathematicians have extended this aspect of Wiles' work, offering a proof of the Taniyama-Shimura conjecture for all elliptic curves rather than just particular types.

The Taniyama-Shimura theorem "is one of the major results of 20th-century mathematics," says Joe P. Buhler of the Mathematical Sciences Research Institute in Berkeley, Calif. "It verifies a truly surprising connection between disparate objects and, along the way, has all sorts of consequences in number theory."

An elliptic curve is not an ellipse. It is a solution of the equation $y^2 = x^3 + ax^2 + bx + c$ (where a, b, and c are constants), which can be plotted as a curve. In general, values of x have corresponding values of y. Number theorists are interested in the specific instances when x and y are both fractions, or rational numbers. In the 1950s, Japanese mathematician Yutaka Taniyama proposed that every rational elliptic curve is a disguised version of a complicated, impossible-to-visualize mathematical object called a modular form. Goro Shimura, now at Princeton, refined the idea.

Elliptic curves and modular forms are mathematically so different that mathematicians initially couldn't believe that the two are related. Wiles verified part of the Taniyama-Shimura conjecture by showing that many types of elliptic curves can indeed be described in terms of modular forms. His proof of Fermat's last theorem came as a consequence of this larger effort, since other work had established a link between elliptic curves and Fermat's last theorem (SN: 6/20/87, p. 397).

News that Brian Conrad and Richard Taylor of Harvard University, along with Christophe Breuil of the Université Paris-Sud and Fred Diamond of Rutgers University in New Brunswick, N.J., had tackled the Taniyama-Shimura conjecture for all elliptic curves appeared earlier this summer. "The proof is complete," Conrad now says. Parts involving intricate computations and various technical details have already been independently checked, and a lengthy paper describing the proof is nearly ready for distribution. —*I.P.*

Crunching Internet security codes

The so-called RSA encryption scheme is widely used to safeguard credit card numbers and other information transmitted across the Internet. To unscramble intercepted data, a snoop's computer must factor a large number into its two prime-number components. If the number is large enough, this task is prohibitively time-consuming (SN: 10/3/98, p. 217). A team of researchers has now demonstrated that numbers consisting of 155 decimal digits (or 512 bits), typically used for securing commercial Internet transactions, no longer provide adequate protection.

Using a worldwide network of computers and a sophisticated mathematical technique called the Number Field Sieve, Herman te Riele of the National Research Institute for Mathematics and Computer Science (CWI) in Amsterdam and his coworkers succeeded in factoring a 155-digit number into two 78-digit primes. The effort took 5 months on 300 personal computers and a Cray 916 supercomputer.

Although such a feat is currently beyond the capability of an ordinary snooper's computer, projected increases in computer speed could make it feasible in 2 or 3 years. Companies involved in Internet commerce are already considering the possibility of switching to RSA schemes requiring as many as 309 decimal digits (1,024 bits). —*I.P.*

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