New test homes in on evasive Lyme disease

A powerful laboratory technique frequently used in basic research reliably identifies trace amounts of DNA from the spiral-shaped microorganism that causes Lyme disease, according to government scientists. The finding should help researchers develop a diagnostic test for this elusive disorder, and may help unlock the mechanism underlying the disease.

Lyme disease gets its name from the Connecticut town where researchers first investigated a cluster of adults and children who suffered periodic bouts of flu, arthritis and neurological problems. Physicians now recognize these as classic symptoms of Lyme disease, caused by *Borrelia burgdorferi* bacteria (SN: 3/25/89, p.184). Yet doctors still have trouble confirming the diagnosis. At present they must rely on blood tests to detect antibodies to *B. burgdorferi* – an unreliable method because some infected people display few, if any, such antibodies.

Patricia A. Rosa and Tom G. Schwan of Rocky Mountain Laboratories in Hamilton, Mont. (part of the National Institute of Allergy and Infectious Diseases) used a technique called polymerase chain reaction (PCR) to develop a test so sensitive that it can detect *B. burgdorferi* DNA in a sample containing as few as five spirochetes. That sensitivity is important because many Lyme patients have very few spirochetes in their blood or tissues.

The team first identified a target DNA sequence present in *B. burgdorferi* and then devised two DNA segments that home in on and bind with the target DNA. Adding the enzyme polymerase, which copies the original DNA target, prompts a chain reaction that generates millions of copies of the target, revealing the presence of spirochetes even in samples containing trace amounts of genetic material.

The scientists report in the December Journal of Infectious Diseases that the PCR test picks out DNA from slightly different strains of *B. burgdorferi*. The test reacted with 17 of 18 strains tested – a significant finding because many people infected with a slightly unusual strain slip through current diagnostic tests, Rosa says. The PCR test proved highly specific, reacting only with material from *B. burgdorferi* and not with DNA taken from a close relative known as *B. hermsii*, which causes a disease called relapsing fever.

A number of researchers already are applying these results in a race to develop a commercial PCR test for Lyme disease. That effort will take at least six months, estimates W. John Martin of the University of Southern California Medical Center in Los Angeles.

Rosa and Schwan plan to use PCR to find out why some Lyme patients develop severe complications such as neurologic and heart problems. One theory suggests those problems result because the bacterium changes to a form the immune system cannot recognize. Another theory holds that the heart and nerve damage comes from an autoimmune process triggered after the immune system conquers the initial infection. PCR would show whether patients with late-stage Lyme disease still harbor any form of *B. burgdorferi*, Rosa says. – *K.A. Fackelmann*

Molecular custodians sweep away odorants

The nose earns its keep by translating chemical stimuli into neural signals that ultimately convey, say, the smell of smoke or lasagna. Biochemically minded neuroscientists get paid for uncovering the molecular details of such feats.

In a seminar this week at the National Institutes of Health in Bethesda, Md., Israeli researcher Doren Lancet described studies at his lab and elsewhere revealing previously unrecognized biochemical players in the complex molecular dance underlying the sense of smell. Lancet, of the Weizmann Institute of Science in Rehovot, reports discovering several enzymes in the olfactory system's patch of receptive tissue – called the olfactory epithelium – that closely resemble detoxification enzymes found in the liver and other body tissues. These olfactory-specific enzymes might be responsible for clearing molecular odor stimuli from the sensory tissue, Lancet says.

Most odorants are volatile, water-avoiding chemicals that readily penetrate oily cell membranes. As such, Lancet says, they should easily spread throughout the sensory epithelium, continuously stimulating the sensory cells. Yet electrode recordings from odorant-stimulated frog and rat olfactory tissue show that the cells stop responding within about a second after the odor source is removed.

Scientists have long imagined that this paradox might be solved by specific enzymes that transform odorants into nonodorants or remove them from the olfactory system. Lancet and his coworkers may have found some of those enzymes. "We identified several detoxification enzymes in the olfactory epithelium," he says. One is an olfactory-specific form of cytochrome P450, a group of enzymes found in many body tissues that help detoxify chemicals that would otherwise remain inside cells to do biochemical mischief. The other is an olfactory-specific form of a different class of detoxification enzymes, known as the uridine diphosphate glucuronyl transferases, or UDPGTs. These typically pick up where a cytochrome P450 leaves off, transforming a water-avoiding molecule into a water-loving form readily cleared from tissue.

Lancet says he suspects that these enzymes, and similar ones still to be discovered in olfactory tissue, change excess odorant molecules into odorless, water-soluble forms that clear from the sensory epithelium. The researchers find the odor-eating enzymes in the glial cells that surround and support the sensory cells and in mucus-secreting cell assemblies called Bowman's glands, also located in the epithelium.

The resemblance of the olfactory forms of cytochrome P450 and UDPGT to known detoxification enzymes is not casual, Lancet suggests. In addition to helping clear out odorants, they may play a role in disarming potentially harmful chemicals, just as their enzymatic kin do in other tissues. Sensory epithelium is a penny-thin barrier between the nasal cavity and the brain, Lancet points out. "Wouldn't it be important," he asks, "for olfactory epithelium to carry a detoxification device such as these two enzymes in large amounts?" – *I. Amato*

'Preshock' pattern may foretell quakes

Investigations of the Oct. 17 Loma Prieta earthquake in northern California hint at a pattern that may help scientists predict some major quakes one to several years before they strike, seismologist Karen C. McNally reported this week at a meeting of the American Geophysical Union in San Francisco. At the same session, other researchers discussed why most structures fared so well in the quake while others collapsed.

McNally, from the University of California, Santa Cruz, observed a trend in the moderate-sized shocks occurring in the year and a half before the Bay area's magnitude 7.1 quake, and noted that the same pattern preceded a magnitude 5.8 temblor in 1986 near Livermore, Calif. In both instances, after a long period of quiet, a series of progressively deeper and larger "preshocks" led up to the main shock.

"I find this an encouraging lead in our effort to track down earthquakes," McNally says. She adds, however, that much more work is needed to determine whether this progression represents a chance occurrence or a reliable sign of an impending quake.

Loma Prieta, the strongest earthquake in the Bay area since 1906, was centered beneath the Santa Cruz mountains, striking the San Andreas fault at the south-