Biomedicine

New gene for heart rhythm abnormality

An international team of researchers has nabbed the third gene associated with an inherited heart rhythm abnormality that can kill otherwise healthy young people.

About 20,000 people in the United States have the heart arrhythmia known as long QT syndrome, which causes episodes of fast, irregular heartbeats that can lead to fainting and sometimes death. The syndrome gets its name from an abnormally long QT interval—the time between heart contraction and relaxation—on an electrocardiogram.

Last year, geneticist Mark T. Keating, a Howard Hughes Medical Institute investigator at the University of Utah in Salt Lake City, and his colleagues identified two genes, on chromosomes 3 and 7, associated with the syndrome (SN: 3/11/95, p. 149). At the time, they also had evidence that mutations in a third gene, on chromosome 11, accounted for about 55 percent of inherited cases of long QT syndrome.

Keating and his team have now identified the third gene, they report in the January NATURE GENETICS. All three genes provide blueprints for proteins essential to the heart's rhythmic contractions.

The chromosome 3 gene codes for a sodium channel, a protein needed to spur heart contractions. In contrast, the chromosome 7 gene codes for a potassium channel, required for halting contractions. The newly discovered gene appears to hold the instructions for another potassium channel.

"Essentially, the sodium channel serves as a gas pedal, and the potassium channels serve as the brakes. If either gets out of control, the result can be life-threatening arrhythmias," says Keating. He notes that physicians can identify the gene mutations responsible for long QT syndrome and target treatments specifically to the sodium channel or the potassium channel.

"Understanding long QT syndrome may one day help us treat the more common arrhythmias, which kill 300,000 to 400,000 Americans each year," Keating adds.

Curable infection linked to early birth

Pregnant women suffering from a common vaginal infection are 40 percent more likely to give birth to premature, low-birthweight infants than are uninfected pregnant women.

Two studies published in the Dec. 28, 1995 NEW ENGLAND JOURNAL OF MEDICINE indicate that bacterial vaginosis—a condition in which various unwanted bacteria displace normal vaginal bacteria—increases the chances of premature birth. Common antibiotics can cure the infection and reduce the risk.

"This condition is a preventable cause of preterm birth," says Sharon L. Hillier of the University of Pittsburgh's Magee-Women's Hospital. "Unfortunately, it is not taken very seriously by health care providers."

Hillier led a team of U.S. researchers that studied 10,397 pregnant women. Overall, 16 percent of the women had the infection, whose symptoms include a fishy odor and excessive vaginal discharge. Six percent of infected women gave birth to premature infants, whereas only 4 percent of the women without the infection had preemies.

John C. Hauth and his colleagues at the University of Alabama at Birmingham studied 624 women who were at high risk of giving birth prematurely because they either were very thin or had a history of premature births. The researchers gave standard antibiotic treatment or a placebo to the participants, regardless of whether they showed symptoms of infection. Of the women later documented to have had bacterial vaginosis, one-third delivered prematurely after the treatment, whereas half of those in the placebo group had preemies.

Hillier recommends that pregnant women mention any symptoms of vaginal infection to their doctors and get treatment if they have bacterial vaginosis.

Chemistry

Treelike molecules branch out

Hugging the Chippewa River some 130 miles southeast of Michigan's Sleeping Bear Dunes, a tree farm sprawls across the plains. Thousands of trees start life there as seedlings before branching into tall, elegant adults.

"Watching these trees with the eyes of a young chemist," says Donald A. Tomalia, now a researcher at the Michigan Molecular Institute in Midland, "I began to wonder whether one could make large molecules the same way."

In 1980, Tomalia synthesized the first dendrimer molecule, its name derived from the Greek *dendron*, or tree. At first, he could only produce small quantities of limited variety. Unlike crystals, which grow into ordered lattices, dendrimers accumulate additional material in a repeating, branched pattern. The structure and composition of the starting material determine the branching pattern.

Other chemists showed little interest in dendrimers until about 5 years ago, when powerful mass spectrometers and the need for specialized molecules produced an explosion of activity around the world. Today, "we're able to create macromolecules on demand with a wide range of sizes, shapes, and weights," Tomalia said at a meeting of the Council for the Advancement of Science Writing in Durham, N. C. "We're learning to produce these materials in kilogram quantities, in some cases up to thousands of pounds."

Just as a tree sprouts successive generations of branches, Tomalia says, these macromolecules branch in stages. Yet, unlike a tree, which produces its building materials internally, the growing molecular structure harnesses smaller molecules from solution at each juncture and fixes them in place according to a branching pattern. "In the end," he says, "you get a macromolecule that resembles a tree."

Unlike most polymers, which form randomly, dendrimers evolve into carefully constructed geometries with specified molecular masses and electronic structures. Such specificity distinguishes these polymers from other synthetic chain molecules and enables chemists to use dendrimers to construct even more complicated macromolecules.

"The dendrimers can grow two, three, four, five, or six limbs at each branching juncture, depending on how the molecule is designed," he says.

"Each time you change the dendritic architecture, you produce new materials with new properties and applications," he says. Because their complex forms are similar to those of many biological molecules, some dendrimers may prove useful in medicine, including genetic and immunological therapies. Others may lead to better microelectronics and plastics.

Virtual reality on a nanometer scale

To study a surface at the level of individual atoms, scientists can call upon a variety of scanning probe microscopes. Using a tiny, computer-controlled stylus that skates upon surfaces to sense atomic forces, these microscopes generate pictures of a specimen's atomic structure.

To enrich this process, Russell M. Taylor II of the University of North Carolina at Chapel Hill has linked a virtual reality display to a scanning probe microscope so scientists can view, feel, and manipulate objects under study.

The system uses a graphics supercomputer and a force-feedback device to give "the illusion of a physical surface floating in front of the user," Taylor said at a meeting of the Council for the Advancement of Science Writing in Durham, N.C.

Donning computerized goggles and gloves, a scientist becomes immersed in a three-dimensional atomic world, experiencing the nooks and crannies of a virus or the tiniest elements of a computer chip. The researcher can then push and pull such nanometer-sized objects.

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