New Theory on the Origin of Twins

Identical twins result from tiny genetic mutations within a developing embryo that lead one portion of the embryo to reject the other as foreign, causing the two to split, a researcher proposed last week at a conference of geneticists. Other scientists, while intrigued by this concept, caution that the supporting evidence remains inconclusive and that further studies are needed to confirm the theory's accuracy.

Judith G. Hall, a pediatrician and geneticist at the University of British Columbia in Vancouver, says she has found genetic dissimilarities between two twins that arose from the same fertilized egg. One twin has developed as a dwarf, while the other has attained normal height and body proportions, Hall reported at the Short Course in Medical and Experimental Mammalian Genetics at Jackson Laboratory in Bar Harbor, Maine. She hypothesizes that this difference resulted from a mutation in one part of the embryo that caused it to split, creating two different "identical" twins.

Fraternal twins and identical twins result from two separate processes. In the case of fraternal twins, a woman releases two eggs in one month. The two eggs are then fertilized by two different sperm. The two resulting fetuses are no more similar than other siblings, although they are almost always born together. Identical twins, on the other hand, are known to result from a single egg fertilized by a single sperm.

For years, geneticists have believed that such twins are genetically, as well as physically, identical. But they have had few theories to account for why a single fertilization event sometimes results in two fetuses.

"There really is no substantiated theory as to what causes [identical] twinning," says Kenneth Lyons Jones, a pediatrician at the University of California, San Diego.

Hall now proposes that all so-called identical twins are really subtly different genetically and that this difference is what causes the embryo to split in the first place. However, she asserts, physicians would detect the tiny genetic difference only in the rare instance when the mutation responsible for twinning happened to disrupt a crucial gene, leading to a disease in one twin but not in the other.

The dwarf twin from the set Hall studied has diastrophic dysplasia, a genetic disorder thought to result from mutations on chromosome 5. Hall hypothesizes that this dwarf twin arose very early in embryonic development, when a single cell of the embryo developed the mutation spontaneously and the other cell or cells ousted that cell as foreign.

"Some of the cells looked at another and said, 'You don't belong here, get out of here,'" suggests Hall.

Once on its own, the expelled cell developed into a complete fetus — identical to its twin except for the mutation, Hall believes.

Victor McKusick, a medical geneticist at Johns Hopkins University in Baltimore — and an identical twin himself — counters that Hall's theory poses a potentially unanswerable dilemma similar to the question of which came first, the chicken or the egg. "Whether the difference [between the embryo's cells] came first or the split came first isn't clear," he contends.

McKusick suggests that the dwarf twin might have resulted from a so-called somatic mutation in one cell *after* the two twins had separated. If this mutation occurred early enough — say, at the eight-cell stage — most of the affected twin's cells would later contain the mutation, possibly leading to a medical disorder, he says. McKusick notes that other geneticists have recorded instances in which one of two otherwise identical twins has Turner's syndrome — a developmental disorder that results from having only one X chromosome instead of the normal XX for girls and XY for boys. However, he concedes that Hall "would read other significance into this" as support for her theory.

Linda Corey, a genetic epidemiologist at Virginia Commonwealth University in Richmond, agrees with McKusick. "The [study's] sample size is a little small to draw the type of conclusions [Hall is] drawing," she adds. Corey, who also directs the Virginia state twin registry, says researchers are only beginning to do detailed comparisons of twins' genetic material to look for the mechanism of twinning.

Jones, on the other hand, advocates a wait-and-see attitude. "I don't think [Hall's theory is] totally off the wall," he says. — *C. Ezzell*

Genetically engineered fungus fights blight

Once a dominant tree in eastern North America, the mighty American chestnut was felled by a fungus introduced from Asia at the turn of the century. Now, molecular biologists have developed a strategy for disarming this fungus so that a new generation of chestnuts may one day tower in the forest.

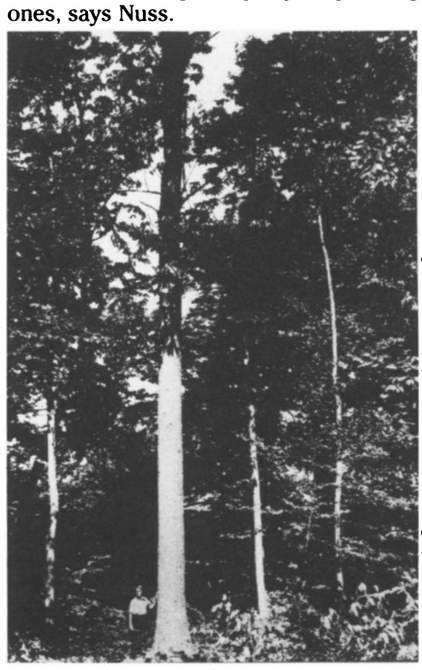
The strategy improves upon the use of a less deadly strain of chestnut blight to neutralize killer strains. Rather than destroy bark and make the tree wilt and die, this "hypovirulent" strain causes only superficial, temporary sores on the bark, says Donald L. Nuss of the Roche Institute of Molecular Biology in Nutley, N.J.

A viral infection reduces this fungal strain's ability to destroy the tree, Nuss and Roche colleague Gil H. Choi report in the Aug. 7 SCIENCE. By making DNA that encodes the virus' RNA, Nuss and Choi plan to harness this virus — or an improved version of it — for controlling chestnut blight.

"It's a new and novel approach for a pathogen that's devastating," comments James L. White, a biotechnologist with the U.S. Department of Agriculture in Hyattsville, Md. "For fungal biocontrol, [this strategy] may be very important."

For more than a decade, plant pathologists have recognized that the less deadly chestnut blight contains double-stranded RNA — a virus of sorts — in its cells. Nuss and Choi proved that this virus renders the fungus hypovirulent.

They began by piecing together a gene for the virus' RNA. When they transferred that gene to virulent fungus, the fungus underwent a transformation: Like the hypovirulent strain, it made less orange pigment and less of certain enzymes. The transformed fungus also caused small cankers to develop on a chestnut stem rather than large, rapidly expanding ones, says Nuss.



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American chestnut tree.

When they examined the fungal tissue, Nuss and Choi discovered that the gene did lead to the production of viral RNA.

Some plant pathologists have treated blighted chestnuts with naturally hypovirulent fungus. That fungus sends out threads that merge with the blight fungus, infecting it with the virus and making it less damaging. But in North America, the fungi are often too different for their tissues to fuse, so the treatment fails.

"We're introducing the virus in a new way," Nuss says. The scientists plan to spray spores from the genetically altered hypovirulent fungi onto infected trees.

Now that the virus' genetic information is transferred along with fungal DNA during sexual reproduction, "we can introduce the virus into any strain," says Bradley I. Hillman, a plant virologist at Rutgers University in New Brunswick, N.J. "It effectively expands the range of the virus [so it infects more strains]."

Next, Nuss and Choi plan to study whether modifying the fungus changes what species of tree it will attack. Then they will apply to the U.S. Department of Agriculture for permission to treat blighted chestnuts in field tests. Other researchers have experimented with altered viruses for insect control, but the new tests would represent the first use of bioengineering to harness a virus to control a fungus, says White.

Nuss and Choi are also modifying this gene to improve the virus' ability to disarm the fungus. In addition, they plan to make genes encoding viruses that can control the fungi responsible for Dutch elm disease and certain crop diseases. At the same time, they hope to use such viruses to learn more about how fungi do their damage. — *E. Pennisi*

Energetic gammas from beyond the galaxy

For the first time, astronomers have detected high-energy gamma rays — photons millions of times more energetic than the most powerful X-rays — from an object outside our galaxy.

The source, a quasar-like object at the center of an elliptical galaxy called Markarian 421, lies some 400 million light-years from Earth. Although the core of this compact object has roughly the diameter of the solar system, its gamma ray output is about 10 million times the sun's total luminosity at all wavelengths, researchers say.

Using ground-based telescopes that detect visible light produced when high-energy gamma rays self-destruct in Earth's atmosphere, astronomers had previously examined likely extragalactic sources of this radiation, including quasars and active galaxies. But such gamma rays — with energies of about 1 trillion electron-volts — turned up only in the Milky Way, most notably in the Crab nebula (SN: 4/28/90, p.270).

When the Earth-orbiting Compton Gamma Ray Observatory (GRO) recently detected lower-energy gamma rays from 14 objects outside our galaxy, Trevor C. Weekes of the Whipple Observatory in Amado, Ariz., and his colleagues decided to examine several of the sources with a telescope that could infer the presence of gammas about 1,000 times more energetic.

Because gamma rays can't survive in Earth's atmosphere, only satellites such as the GRO can detect them directly. But the small detectors aboard such craft have difficulty recording the relatively low abundance of very energetic gammas, Weekes notes.

Though the data suggested that Markarian 421 was not the most intense high-energy gamma ray emitter among the 14 sources GRO had identified, that galaxy does reside closest to Earth. And in observing this galaxy with a gamma ray telescope at the Whipple Observatory last spring, Weekes and his colleagues found the extragalactic emissions they had long been searching for. They report their results in the Aug. 6 NATURE.

Researchers have suggested that previous searches for trillion-electron-volt gamma rays from more distant galaxies had failed because such radiation is easily absorbed by the fog of infrared starlight in the intergalactic medium. Weekes notes that the gamma radiation generated by Markarian 421 probably comes from the edges of a jet believed to emanate from a quasar-like entity, called a BL Lac object, at the galaxy's center. Energetic protons colliding with other particles in the jet may generate the gammas, he speculates.

In a commentary accompanying the NATURE article, Francis Halzen of the University of Wisconsin-Madison says that Markarian's gamma ray output suggests that the galaxy may emit an even higher intensity of elusive subatomic particles called neutrinos. — *R. Cowen*

Male cancers raise women's breast risks

Women with a mother or sister stricken with breast cancer run a higher-than-average risk of developing the disease themselves. A new study now puts a surprising twist on that well-known fact: Women should also look to male relatives for hints of a breast cancer threat.

In the United States this year, about 1,000 men will develop breast cancer and 300 will die of the disease. Investigators have tried to learn whether female relatives of men with breast cancer run a high risk of the illness, but the studies have yielded conflicting results.

David E. Anderson and Michael D. Badzioch of the University of Texas M.D. Anderson Cancer Center in Houston decided to take another look at the families of male breast cancer patients. They focused on 88 men admitted to M.D. Anderson Cancer Center from 1958 through 1989 with a diagnosis of breast cancer. The investigators contacted the patients or a family member to find out whether any of the patients' first-degree female relatives — mothers, sisters, or daughters — had breast cancer. They confirmed each reported cancer case by examining the medical records or contacting the family's physician. Next, they compared the observed number of breast cancer cases with the expected number by getting data from a tumor registry that records breast cancer rates in the general population. Their analysis revealed that first-degree female relatives of male breast cancer patients run twice the expected risk of breast cancer.

The Texans also looked at the number of breast cancer cases recorded among the close female relatives of 186 female breast cancer patients. These relatives, too, faced double the expected risk of developing breast cancer, according to the team's report in the July 15 JOURNAL OF THE NATIONAL CANCER INSTITUTE.

The new findings suggest that physicians assessing the risk of breast cancer should ask women whether any of their close relatives — male or female — have had breast cancer. Epidemiologist Karin A. Rosenblatt of the University of Illinois at Urbana-Champaign agrees, but notes that male breast cancer is so rare that such questions will only infrequently turn up an affected relative.

In the course of their study, Anderson and Badzioch also turned up an unexpected link between a family history of prostate cancer and the risk of breast cancer. They found that women faced a four-fold increased threat of breast cancer if a male family member had a history of prostate cancer.

Anderson believes physicians should ask women about a family history of prostate cancer, as it seems to substantially increase the odds of breast cancer. On the other hand, Louise A. Brinton of the National Cancer Institute in Bethesda, Md., argues that researchers must confirm this finding before doctors change the way they gauge women's breast cancer risk.

The research raises the possibility that a cancer-causing gene or genes run in some families, predisposing some people in the family to breast cancer and others to prostate cancer, Anderson says. He notes that scientists have yet to unravel the mechanisms underlying breast and prostate cancer. — *K.A. Fackelmann*