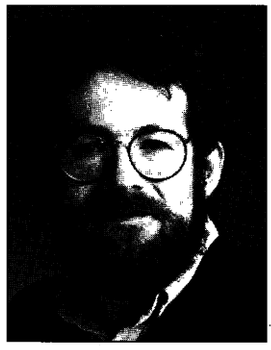
elements and filling in each position of the consensus sequence with the base that most commonly occupied it. Beth Dombroski, a postdoctoral fellow in Kazazian's laboratory, then searched for the biggest distinction she could find between the child's transposon and this consensus sequence. One 20-base stretch had three base changes, a difference of 15%. Human LINEs typically vary by no more than 5%. She had her handle.



Working gene. *Abram Gabriel showed that reverse transcriptase is produced.*

Using this 20-base sequence as a probe, Dombroski found five LINEs in the mother's DNA that closely matched the transposon sitting in the child's factor VIII gene. The child's transposon proved to be a truncated version of one of these, a full-length LINE on chromosome 22. They are identical in all bases that had not been deleted. Dombroski subsequently found this LINE in the same position on the father's chromosome 22. "As far as we know, everybody's got it in that location. We've even found it in the same location in chimps and gorillas, which means it's been at the same place in the genome for at least 6 million years," says Kazazian. It's impossible to say whether the mother's or the father's transposon was the progenitor, he adds.

The next step was to see whether the transposon could make reverse transcriptase. Active LINE elements are copied into RNA, which is then converted into a DNA copy by reverse transcriptase. The DNA copy is then inserted into a new place in the genome. Gabriel, along with graduate student Stephen Mathias and associate professors Scott and Boeke, tested the transposon's reverse transcriptase gene by splicing it into the equivalent region of a yeast transposon, and then showing that particles taken from the yeast cytoplasm have reverse transcriptase activity. They nailed down the proof by making a point mutation in the reverse transcriptase gene, which disabled the protein.

The fact that the child's transposon is a truncated version of that of its parents' suggests that the deletions so common among mammalian LINEs are acquired during jumping. "That answered a question as to whether the degeneration is something that happens in the course of evolution or whether it is part of the process of transposition," says Maxine Singer, president of the Carnegie Institute of Washington, a longtime expert in this field. Some researchers think that these crippling mutations may be nature's way of controlling the population of transposons.

Perhaps the biggest unanswered question is what role transposons play in the human genome. Many researchers think they are genetic parasites, whose presence in the genome is harmful to the organism. But some think that organisms may have become dependent upon them over the course of evolution. "There is something interesting about the fact that all mammals have retained these sequences, in spite of the fact that they are mutagenic," says Singer.

An interesting angle for future research, suggests Singer, is the possibility that LINEs may play an important role as a source of reverse transcriptase in the genome—a role that may help *Alu* sequences move around and, in turn, might be a major factor in the evolution of the genome. Because *Alu* sequences (and similar sequences in other organisms) lack reverse transcriptase genes, they have no obvious means of transposing themselves to new places in the genome. But the research at Johns Hopkins suggests that LINEs could be providing the enzyme. "There is no other known consistent source of reverse transcriptase in mammalian genomes," says Singer, though endogenous retroviruses may occasionally provide the enzyme. "It is very possible, since we know that various pieces of DNA have arisen in the genome through reverse transcriptase, that this is the enzyme that did it," she adds.

The scattering of *Alu*, LINE, and other repetitive sequences around the genome may play a role in duplicating genes in the genome, which is thought to be important in the development of whole families of genes such as the hemoglobins, the individual members of which have somewhat different functions from one another. (Duplicate genes can develop new functions because mutations in one won't kill off the host organism.)

Duplication can occur during meiosis, when an unequal genetic cross-over takes place between two paired chromosomes. In a normal cross-over, the chromosomes trade genes, but in an unequal cross-over, one chromosome can end up with two copies of a gene, leaving the other with none. That's where repetitive sequences come in. If a gene is flanked on both sides by repetitive sequences, base pairing between these sequences can occur so readily that it pulls the DNA into a configuration that leaves both copies of a gene on one chromosome. Without reverse transcriptase, *Alu* sequences could not have multiplied in the genome to the point where genes are sometimes surrounded by them. LINE elements may complete this story. ■ DAVID HOLZMAN

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HIV Risk Higher for First-Born Twins

For twins born to HIV-infected mothers, the first child delivered is more than twice as likely to be infected with the virus as the second. That's the remarkable—and potentially controversial—result of an international study published last week (*Lancet*, 14 December, p. 1471). The finding strongly suggests that in most instances, the AIDS virus is transmitted from mother to infant at birth. If it were transmitted across the placenta earlier in pregnancy, birth order should make no difference in the incidence of transmission.

The study compared 66 pairs of twins delivered either vaginally or by Caesarean section. For vaginal births, 50% of first-born twins were infected with HIV, compared to 19% of second-born twins. In Caesarean births, the effect was smaller and not statistically significant: 38% for the first born twin, and again 19% for the second born twin. James J. Goedert, a member of the viral epidemiology section of the National Cancer Institute and senior author of the study, postulates that the first-born infant must come in contact with some maternal fluids released at birth that contain infectious virus. But in the process of delivery, most of that fluid is swept away, so the second infant is less likely to be exposed to infection. Goedert says that simply cleansing the birth canal may reduce the transmission rate of the virus from mother to infant.

But others are not convinced that the majority of transmission occurs at birth. William Lyman, associate professor of pathology at the Albert Einstein College of Medicine in the Bronx says he finds a 30% infection rate in second trimester fetuses carried by HIV-infected mothers. Lyman acknowledges that infection across the placenta may be enhanced in his patient population because many of the mothers he studied were also crack-cocaine users. Cocaine use is associated with vasculitis, which may permit leaks between the fetal and maternal blood supply.

Goedert is accruing more patients and plans to take an additional look at infection rate and birth order in about a year to see if the results hold up. ■ JOSEPH PALCA