

Jumping Genes in Corn

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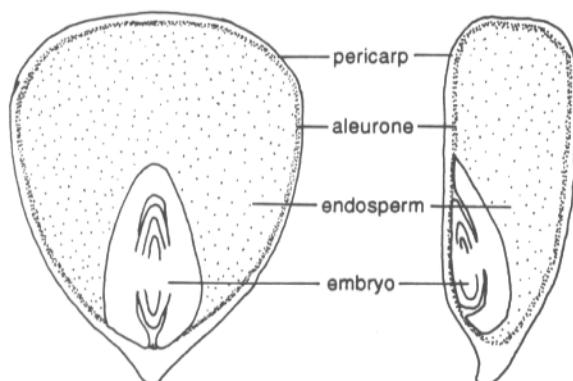


Background Reading

Activity I: Simple Inheritance

Each kernel on an ear of corn is a potential corn plant. It contains an embryo resulting from the union of two gametes, one (the egg) contributed by the female plant part and the other (the sperm) contributed by the male plant part.

The structure of a corn kernel is illustrated below. It includes a thin outer layer, the pericarp; a thin underlying aleurone, which is the outermost layer of the endosperm; the remainder the endosperm, which contains the kernel's stored food; and the embryo. Each of the three outer layers may be pigmented or not, with the presence or absence of pigmentation being under the control of several different genes.



Drawing adapted from Fedoroff, N.V. (1984). *Scientific American*, 250(6), 85-98.

The chemical form of food stored in the endosperm affects the appearance of the kernel. This is under genetic control, with the *Su* gene for starchy (smooth and rounded appearance) being dominant to the *su* gene for sweet (wrinkled and raisin-like).

Each of the three outer layers may be pigmented or not. Pigmentation in the aleurone layer is under control of a number of genes. In Activity I, you will be concerned with only one of these genes, the *R* locus. *R* is dominant to *r* and causes a purple or red color; the *r* allele does not cause any pigmentation of the aleurone.

Activity II: Complex Inheritance

Pigmentation in the aleurone layer is actually under the control of at least three different genes, *R*, *Pr* and *C*, each of which may occur in different forms, or alleles. At the *R* locus, allele *R* allows color to be present in the aleurone; *R* is dominant to *r* which does not produce a pigment. The expression of a second set of alleles at a different locus, the *Pr* locus, varies with whether the *R* or *r* allele is present. *Pr* produces purple color, while *pr* contributes red. *Pr* is dominant to *pr*. In order for the *Pr* locus to be expressed, there must be at least one *R* allele present. If there are at least one *R* gene and one *Pr* gene (i.e., a *Pr_R_* genotype) then the kernel can be purple; a genotype of *prpr R_* can produce a red aleurone; *rr* contributes no color to the aleurone. The relationship between the *R* and *Pr* loci is an example of epistasis, a condition that results when genes at one locus affect the expression of genes at another locus.

Note that we said the aleurone **can** be purple. Aleurone color is affected by yet another locus, *C*, which provides an example of both epistasis and multiple alleles. In order for the aleurone to be pigmented, there must be at least one *C* allele at the *C* locus, i.e., *CC* or *Cc*. A *cc* individual will lack aleurone pigmentation. Besides *C* and *c*, there is another allele *C¹*; it is dominant to *C* and prevents any color from being expressed in the aleurone. For instance, a *PrPr RR C¹C* individual would lack aleurone coloration. A locus with more than two alleles is said to be under the control of multiple alleles.

Another locus that is involved in determining the color of corn kernels is the *Y* locus. This is a case of simple dominance, with *Y_* producing yellow endosperm and *yy* producing white endosperm. The color of the endosperm is often not visible because of the overlying purple or red pigments in the aleurone.

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Activity III: Jumping Genes and Inheritance

For the first part of this century geneticists believed that genes were static with regard to their positions on chromosomes. Work first reported by Barbara McClintock in 1947, however, revealed that genes could indeed move within and between chromosomes. McClintock kept careful records of genetic crosses in corn and observed the color changes on individual kernels of ears of corn over numbers of generations. From her data, she concluded that there must be genetic elements that could move to and be inserted at the loci for color in corn kernels. These fragments of DNA are now called transposons, or transposable genetic elements. When she published her unorthodox work in the early 1950s, it was discounted as impossible because it did not support the hypothesis under which all other geneticists were operating, that is, that the position of genes was fixed. Her work was later corroborated by findings of similar phenomena in bacteria, yeast, fruit flies and mammalian retroviruses. She received the Nobel prize for her work in 1983.

Specifically, McClintock showed that there was a genetic element which could move to and be inserted at the C locus. Insertion of this Ds element (for dissociation, so named because it was frequently a site of chromosome breakage) rendered the C locus unable to contribute to the production of purple pigment in the aleurone; subsequent removal of the Ds element from the C locus allowed the pigment to be produced. Ds did not itself cause the breakage, however; rather this required the presence of another element, called Ac for Activator. If the Ds element (in the presence of the Ac element) moved from the C locus during the development of a kernel, all cells resulting from that cell would be purple. Each cell in which such a translocation took place could eventually result in a purple spot on an otherwise yellow or white kernel of corn.

The P locus was another found to affect kernel color. It was found that the Ac element could insert itself at the P locus, disrupting thereby the production of a red-orange pigment in the pericarp. Translocation to and from the locus several times during kernel development resulted in the red-orange swirls characteristic of many kernels on "Indian corn."

Subsequent studies in corn have revealed other "families" of transposons analogous to the Ac-Ds family. Each family contains elements that, like Ac, can effect their own movement and that of other elements in the family from one site to another. Such elements are called autonomous. In addition, each family generally contains nonautonomous elements that, like Ds, can only move in the presence of an autonomous member of the same family. In many cases nonautonomous elements appear to be derived from autonomous elements by deletion of DNA sequences.



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Materials

Each lab group will need one of the following ears of corn

Activity I:

- ▼ 1 yellow starchy: 1 yellow sweet
- ▼ 3 purple starchy: 1 yellow starchy
- ▼ 9 purple starchy: 3 purple sweet: 3 yellow starchy: 1 yellow sweet

Activity II:

- ▼ 9 purple: 3 red: 4 white
- ▼ 12 purple: 3 yellow: 1 white
- ▼ 13 yellow: 3 purple
- ▼ 2 purple: 1 yellow: 1 white
- ▼ 9 red: 7 white
- ▼ 9 purple: 3 red: 3 yellow: 1 white
- ▼ 3 yellow: 1 purple
- ▼ 9 yellow: 3 white: 4 purple

Activity III:

- ▼ "Indian corn"

Procedure

Activity I:

Simple Inheritance

1. Obtain an ear of corn for your group.
2. Using slides or the ears themselves, point out examples of purple vs. yellow, and starchy vs. sweet kernels.
3. Purple color is caused by pigmented cells in the aleurone. It is under control of a pair of alleles, R which allows the color to be expressed and r which does not allow expression. R is dominant to r. Smooth, round kernels (called "starchy") result from the presence of a dominant gene Su, whereas wrinkled kernels (called "sweet") have the genotype susu.
4. Determine the genotypes of the parents that produced your ear of corn. Hint: Count the number of kernels of each phenotype, then make a Punnett square and "reason backward" to obtain the parents' genotypes. In the interest of time you can count only a few rows rather than the whole ear.
5. Choose a spokesperson (if working in a group) to present your results in a whole class discussion.

Activity II:

Complex Inheritance

1. Obtain an ear of corn for your group.

2. Make sure you can distinguish purple, red, yellow and white kernels
3. Use the information in the Background Reading to determine with your group the possible genotypes of purple, red, yellow and white kernels.
4. Determine the genotypes of the parents that produced your ear of corn. Two hints that may be of use to you are:

Hint 1: Look for examples of familiar Mendelian ratios. For instance, an ear that has 9 purple: 3 red: 4 yellow has a non-yellow:yellow ratio of 3:1. Such a ratio could have resulted from crossing two heterozygous parents $Rr \times Rr$. In addition, the ratio among the non-yellow kernels is 3 purple: 1 red, suggesting parental genotypes of $Prpr \ Rr \times Prpr \ Rr$. The fact that all the kernels lacking aleurone pigment are yellow suggests that at least one parent was homozygous for the Y gene, i.e. $Prpr \ Rr \ YY \times Prpr \ Rr \ _$. These parental genotypes account for the 9:3:4 ratio provided at least one parent was homozygous for C and neither had C^1 , giving one possible answer of $Prpr \ Rr \ YY \ CC \times Prpr \ Rr \ yy \ CC$. What are some other "correct" answers?

Hint 2: As an alternative, it may be helpful to make a Punnett square and "reason backward" to obtain the parents' genotypes.

5. Choose a spokesperson (if working in a group) to present your results in a whole class discussion.

Activity III:

Jumping Genes and Inheritance

1. Obtain an ear of "Indian corn" for your group.
2. Ask each group to look for examples of:
 - kernels with purple or white spots.
 - kernels with red-orange swirls resulting from translocations to/from the P locus.
 - Other color patterns that might be explained by similar genetic mechanisms.
3. Use the information in the Background Reading to determine how:
 - purple or white spots result from translocations to/from the C locus.
 - red-orange swirls result from translocations to/from the P locus.
4. Choose a spokesperson (if working in a group) to present your results in a whole class discussion.

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Questions

1. Assume a corn kernel had the genotype Prpr Rr YY Cc . What color would its endosperm be? What color would the kernel appear to be? Explain your answers.

2. Assume that an ear of corn is produced by the following cross:

$$\text{Prpr RR Yy CC} \times \text{prpr RR yy CC}^1$$

What would the phenotypic ratio of the kernels on the ear be?

3. Assume that the phenotypic ratio on an ear of corn is 9 purple: 7 white. What were the genotypes of the parents?

4. How do you think the C^1 gene prevents pigment from occurring in the aleurone even when the Pr, R and C genes are present?

5. How might transposons be used one day in genetic engineering?

Transposon Tagging of Plant Genes

Clintock and the
Ds Transposable
Elements of Corn

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Elements](#)

[Molecular Features of
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McClintock and the Ac/Ds Transposable Elements of Corn

Barbara McClintock was the first scientist to predict that transposable elements, mobile pieces of the genetic material (DNA), were present in eukaryotic genomes. She performed her work on corn and specifically followed seed color phenotypes. Before we discuss her experiments, it is necessary to describe the morphology of the corn seed and the parental source of the genes which control its phenotype

McClintock discovered transposable elements by analyzing genetic stocks of corn that were phenotypically unstable. In particular, she was analyzing genes that control the color of the aleurone layer of the endosperm. Remember that this tissue is triploid ($3n$). The genes that she was following were located on the short arm of chromosome 9 of corn and were involved in the development of the color of the seed. The genetic map of this region and the allelic designations follow.

C Bz Ds

C' = dominant allele that prevents color from being expressed in the aleurone layer

C = recessive allele that leads to color development in the aleurone layer

Bz = dominant allele that produces purple aleurone color

bz = recessive allele that produces a dark brown to purple-brown aleurone color

ds = a genetic location where chromosome breakage occurs

Homozygous stocks were created and $CC\ bzbz$ -- females (without ds , denoted by the dash) were mated with $C'\ C'\ BzBz$ $dsds$ males. The aleurone layer of the endosperm would thus have the genotype $C'\ CC\ Bzbzbz$ -- ds . Because of the presence of the inhibitor allele, the aleurone layer was expected to be colorless. For many of the kernels this was the case but a few kernels had dark brown colored sectors on an otherwise colorless background.

How could this have occurred? McClintock concluded that in some manner the C' and Bz alleles were lost because chromosome breakage had occurred at the Ds locus. But why the sectoring? This breakage apparently did not occur during gamete formation, but had occurred after fertilization and during the development of the seed. This breakage and loss of genes occurred in a single cell, but all cells that developed from mitotic division of that cell did not contain the inhibitor gene, so the color expression was controlled by the bz allele in those cells.

Female gametes:

$\overline{C\ bz}^{//}$

Male gametes:

$\overline{C'\ Bz\ ds}$

The following is the expected chromosomal composition of triploid endosperm. Because of the dominant C^1 allele the endosperm should be colorless without breakage

C	bz	//	(from female)
C	bz	//	(from female)
C^1	Bz	ds	(from male)

But if breakage at ds occurred, then the genotype of the endosperm would be:

C	bz	//	(from female)
C	bz	//	(from female)
C	bz	//	(from male)

and any cells with this genotype would be dark brown in color.

Breakage at ds had been established by McClintock prior to performing these experiments. The designation ds was short for dissociation or a locus were breakage of chromosomes occurred. But after crossing with a number of different genetic stocks, she realized that Ds alone could not induce the breakage. A second factor, Ac, short for activator, was also necessary. (Thus, some genetic stocks contained Ac whereas other stocks did not contain that locus.) This system is called a two-element system and historically has been called the Ac/Ds system.

Additional genetic stocks were analyzed by McClintock and she determined that in the presence of Ac, Ds could move locations as well as cause breakages. She was able to isolate a corn line where Ds had moved into the normal Bz allele and caused a mutation in that gene. But as was mentioned this only occurred when Ac was present. Furthermore, when this new line was used and Ac was present, the Ds element was shown to move out of the Bz locus and reversion to the original phenotype was detected. This mutated allele was designated bz^{m1} . But in the absence of Ac, bz^{m1} was a stable allele. Another unstable Bz allele was found that contained an Ac insertion and was designated bz^{m2} . One difference between this allele and bz^{m1} was its higher rate of transposition and reversion back to the original phenotype

So what conclusions can be drawn from these experiments and observations:

1. Ds requires some factor provided by Ac to move, whereas Ac is independent
2. Because of their relationship, Ac is termed an autonomous element and Ds a non-autonomous element.
3. Because both Ac and Ds can move, they are called transposable genetic elements.

Transposons

So-called junk DNA proves its worth: First in corn, now in creatures like us

BY AYALA OCHERT

Within three years, if not sooner, the Human Genome Project will be completed, and all 3 billion or so bases of the human genetic code will have been recorded. That's when biologists will face up to an uncomfortable truth: Less than 5 percent of the human genome is likely to contain functioning genes. The rest of it is stuffed—like a stranger's attic—with mysterious relics of an unknown past. Nearly half is parasitic DNA—commonly known as "transposable elements," or simply "transposons," and everything left over is just anonymous noncoding DNA. Over the years, scientists have downplayed the significance of this excess genetic baggage, referring to it disdainfully as "junk" DNA. But now the tide is turning—for transposons at least—as biologists begin to recognize that these tiniest of parasites may have been real players in evolution after all. Without their insidious presence, complex creatures

Transposons, or "jumping genes," can produce color variations in corn kernels by disrupting a gene's normal sequence.



TRANSPOSONS

Transposons are sometimes whimsically referred to as "jumping genes," because they seem to hop from place to place within the genome. There are several varieties of transposon, each with its own method of jumping. The simplest use a cut-and-paste strategy: Their DNA instructs the cell to make an enzyme that can seek out the transposon, pick it up by both ends, and reinsert it at a new location. A

common but more sophisticated variety is the retrotransposon. The cell treats the retrotransposon just like one of its own genes and

How Genes Jump

creates RNA from it. Just after the RNA is assembled, the retrotransposon makes an enzyme called reverse transcriptase, which cunningly converts the RNA back into a DNA copy that is an exact replica of the original transposon. That duplicate then finds a new place along the genome and takes up residence.

The mode of retrotransposon movement is remarkably similar to that of retroviruses like HIV—so similar, in fact, that many scientists believe these viruses must have evolved from retrotransposons. Transposons have also managed to escape from their hosts and move to new ones, sometimes from different species, by a mysterious process called horizontal transmission. Although no one knows exactly how it happens, the transposons probably hitch a ride off an unsuspecting virus that happens to have infected its host. The transposon jumps on board, and it's free.

Entomologist Hugh Robertson of the University of Illinois at Urbana-Champaign has turned up evidence for hundreds of such cases of horizontal transmission, sometimes between very different species. That strategy, he believes, may be the transposon's only means of survival. "Within any particular host, they will eventually die by mutation and become nonfunctional. By jumping to a new host, they get a new lease on life before dying out in the old host." —AYALA OCHERT

like us may never have evolved. These rogue bits of DNA may even have shaped those features that distinguish us from our closest primate kin.

Transposons are not new to biology. In the 1940s, the gifted cytogeneticist Barbara McClintock came up with the idea that DNA sequences are not always static; they sometimes move around from place to place, leaving biological peculiarities in their wake. With this idea, she was able to explain why the Indian corn she was studying didn't inherit coloring in the orderly fashion of Gregor Mendel's peas. Instead, something was causing variations to appear—more or less at random. The changes, McClintock suggested, were the handiwork of mobile genetic elements, which are today known as transposons. Unable to understand her work, other scientists were reluctant to go along with such an unorthodox idea.

By the 1960s, however, McClintock's ideas were gaining ground and, in 1983, she won the Nobel prize for her transposon research. But even now, few scientists have come to terms with just how important transposons might have been during evolution. If anyone truly appreciates their significance, it is John McDonald, a molecular biologist at the University of Georgia in Athens. He believes that without transposons nothing more interesting than a bacterium may have ever crawled out of the primordial mud.

McDonald has devoted his career to understanding the molecular tools of these rogue stretches of DNA, and he knows well their special talent for wreaking havoc in the genome. A few changes in maize kernels may not sound too worrisome, but all too often transposons are far more deadly, and many diseases—including hemophilia, leukemia, and breast cancer—have been linked to their destabilizing influence. What makes transposons so powerful—and dangerous—McDonald explains, is their mobility. Transposons piggyback on their host's genome and are copied hundreds of times over. They get a free ride down through the generations, but as they jump around at will, they can land on vital genes, blotting them out, or land near genes,



Barbara McClintock's research was so original that a colleague exclaimed, "That woman is either crazy or a genius." In 1983, she won a Nobel prize for her work.



The Mortal Coil

Genetic sequences harboring transposons (green) tend to be stowed away in tightly coiled sections of noncoding DNA called heterochromatin. But in coding DNA (light blue), the coiled DNA relaxes, exposing genes for copying. If a transposon happens to jump into coding DNA, it can disrupt normal gene function.

setting them off at the wrong time or in the wrong place [see "How Genes Jump," page 60].

That instability, argues McDonald, has represented a serious threat. Throughout evolution, plants and animals have had to contend with these

unwelcome residents, and the force of natural selection has been a source of constant pressure to clamp down on these genetic freeloaders—to inactivate, or "silence," them, putting a halt to their disruptive spread. "The whole process is dynamic, and trans-

posons are working constantly to escape silencing," he says. "It's a continual battle." McDonald believes that this unseen struggle at the molecular level may ultimately be responsible for two blockbuster events in the history of animal evolution.

The first occurred around two billion years ago, when multicellular creatures like worms and insects began to emerge. The new complex organisms looked different from their simpler predecessors—and their genomes looked very different too. These organisms had many more genes, and they packaged them very differently. Instead of having a loose, lengthy loop of genes, as bacteria do, these creatures had chromosomes—dense packages of DNA and proteins in the form of chromatin. McDonald thinks the need to control rowdy transposons hastened this unprecedented molecular innovation. The new chromosomal packaging allowed the cell to stow away disruptive transposons, yet somehow leave privileged genes available for use. And that ability to control access to genes would improve an organism's ability to manage a complex and varied genome.

The second event occurred around 500 million years ago, when vertebrates like fish, birds, and mammals began to appear. These organisms harbored even more genes, and their genomes were littered with molecular additions called methyl groups (CH_3s). Methylation is still poorly understood, but McDonald thinks it added a second layer of gene inactivation over and above that offered by chromatin. Genes lacking methyl groups tend to be available for making proteins; genes with methyl groups don't. It's as if these molecular ornaments work like a master switch for shutting down inappropriate activity in the genome. Like chromatin formation, methylation may have arisen as a strategy to defend against transposons, says McDonald. And it may be that once mechanisms for shutting down transposons were in place, organisms began using them to control not just invading transposons but their own genes too.

In fact, molecular biologist Adrian Bird of the University of Edinburgh in Scotland has argued that without

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chromatin formation and methylation, complex life would have been impossible. In multicellular organisms with lengthy complex genomes, different cells need to turn different genes on and off. Chromatin formation and methylation—with their ability to alter gene expression—were tools that made such control possible. What McDonald has added to Bird's argument is the role of transposons in prompting the evolution of these genomic features. "If we had to sit around and wait for methylation to evolve for the host function, it would probably never have happened. This molecular battle [between transposons and their hosts] just sped up evolution. It's like technology in society—would it have evolved as fast as it did if it weren't for the military-industrial complex?" he asks.

McDonald's hypothesis is provocative, although there is no way of proving conclusively whether chromatin formation or methylation evolved to inactivate transposons millions of years ago. But McDonald points to intriguing evidence that both chromatin formation and methylation are still important for reigning in transposons. Chromatin, for example, performs the most remarkable feat of packaging known to biology. Within the nucleus of each human cell, nine feet of DNA must be tightly coiled into chromosomes. In its most "condensed" state, the DNA is so tightly bundled up that it's entirely inaccessible to gene-

In the fruit fly *Drosophila*, for example, the constitutive heterochromatin is jam-packed with transposons. And when researchers at the Howard Hughes Medical Institute inserted a few transposons end-to-end along the *Drosophila* genome, they found that new material re-

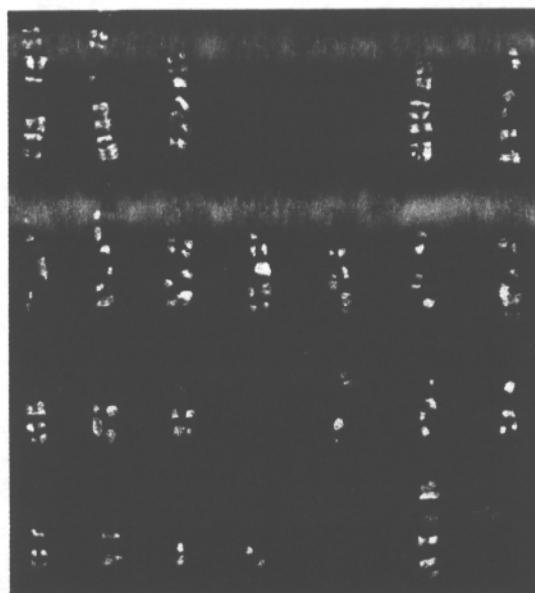
What's more, when the methyl groups are stripped off the genome, these elements actually get reactivated. And there's even more provocative evidence of the policing power of methylation in the human genome. Nearly half of our own genome consists of transposons, yet only 0.2 percent of

all spontaneous human mutations are caused by transposons. In fruit flies, transposons constitute only 10 to 20 percent of the genome, yet they are responsible for as much as 85 percent of spontaneous fruit fly mutations. Methylation may be the key. Our genomes are methylated; fruit fly genomes are not. So, although humans harbor far more transposons than fruit flies, methylation may curb their ability to do us harm.

But, try as it might, no organism can stop every single transposon, and occasionally one will sneak its way past all the genetic checkpoints. Much of the time transposons have no effect, but sometimes they cause an unwelcome mutation. In humans, for example, the movement of transposons from one

point of the genome to another during the formation of eggs or sperm is a constant source of inherited diseases. One in 3,000 people will get type I neurofibromatosis—a disease that can cause café-au-lait patches on the skin, growths, bone deformities, and learning disabilities—and about half of these cases are caused by new mutations, which are then passed on to future generations. In some cases, the exact moment when a transposon disrupted the normal gene has been traced to a single individual, usually a father or grandfather in a family with that disease.

Despite transposons' bad reputation, they have made some surprisingly significant and lasting contributions to the genomes of animals and humans.



The mariner transposon (green) is scattered throughout the human genome, according to a recent study by Lawrence Reiter of the University of California at San Diego and his colleagues. Mariner transposons don't appear to be functional, says Reiter. But they do appear guilty by association: Mariner transposons are found in 12 chromosomal regions that have been linked to genetic disorders.

If transposons move while eggs or sperm form, they can cause heritable disease

activating enzymes. As stretches of chromosome move out of this condensed state, genes are exposed and available for expression. But some sections—known as constitutive heterochromatin—are permanently condensed and packaged away. These sections are like graveyards for transposons.

sembling heterochromatin would spontaneously generate where there was none before. It seems that with all their jumping around and duplicating themselves, transposons made themselves a little too conspicuous. So heterochromatin formed around them, trapping them in place.

There's also evidence that methylation, too, still defends against transposons. Timothy Bestor and his colleagues at Columbia University say that as much as 90 percent of all methylated sequences in the mammalian genome occur in transposable elements.

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A 1998 study by David Schatz and colleagues at Yale, for example, helped explain how the powerful immune system of vertebrates appeared so abruptly in evolution. Almost 500 million years ago, jawed vertebrates acquired the ability to begin producing nearly infinite types of antibodies in response to bacterial or viral invaders. They do so by mixing gene fragments to create a vast array of antibody genes in millions of B cells. This recombination, which occurs very early in development, produces a diverse multitude of antibody sentinels. Schatz and his team found that this incredible genetic flexibility is made possible by the RAG transposon, which fortuitously entered our lineage around 450 million years ago. The RAG creates the protein used to "cut and paste" the gene fragments

movement of transposons has had a much more significant effect than classical mutations—those in which a single base change results in a slightly different protein. When transposons jump to new locations, they can alter patterns of gene expression, and therefore have far more of an effect on how an organism actually turns out. Britten believes that transposons are unsurpassed as a source of natural variation. "You couldn't explain the process of evolution on the basis of single point mutations. You need a more powerful device." That powerful device, he says, is the transposon.

Britten has been particularly interested in how a transposon called the Alu element could affect patterns of gene expression. Alus are unique to primates and, for some unknown reason,

they seem to have spread widely around 30 million to 50 million years ago. Although their period of intense activity occurred long before human-apes ever walked the earth, Alus have left a signature in our genome. Each of us has nearly a million Alus, and they make up more than five percent of our DNA.

In fact, says Britten, the Alu element is the most abundant type of transposon in the human genome. And, according to molecular biologist Wanda Reynolds, the Alu may have played a critical role in our own evolution.

When Reynolds began studying Alu elements at the Sidney Kimmel Cancer Center in San Diego several years ago, she noticed that part of the Alu sequence bore an uncanny resemblance to something she had seen before. She had been working with distinctive DNA sequences that act as anchor points for proteins that bind to hormones. When a hormone is bound in this way, it can switch on a whole set of genes, starting a cascade of biochemical events throughout the body. When the hormone estrogen, for example, binds to such a sequence, it triggers the genes involved in ovulation. Or when growth hormone binds to a similar stretch, it triggers the genes necessary to make a child grow.

These sequences are extremely powerful, so the discovery that they reside in all Alu elements startled Reynolds. As Alus moved around during primate evolution, they would have had the power to alter which set of genes got triggered by which hormone and when. She also found that various Alus bind to several different hormones, including retinoic acid, thyroid hormone, and even estrogen—all of which are critically important in the timing of development.

"These Alus could have generated more diversity—but subtle diversity," says Reynolds. "We're not talking about knocking a gene out, but just slightly elevating or reducing its expression in certain tissues, so that you could gradually change the evolution of the species. Alus were probably very important in primate evolution, because without them you may never have had the diversity from which to select the primates," says Reynolds.

The importance of this subtle diversity becomes clear when you consider the differences between ourselves and our closest living relatives, the chimpanzees. Although they share more than 98 percent of our genes, it is less often acknowledged that such a small distinction can hardly begin to account for the very real differences between how we and they look and behave. "It's not just the sequence of the genes, it must be something about the way genes are turned on, the way they're controlled," says McDonald. "There must be different patterns of expression that are key to the differences in morphology." With their ability to bind hormones and thus switch genes on and off during development, Alus may very well have shaped the evolution of our species.

The more we learn about transposons and their powerful effects, says McDonald, the harder it becomes to think of them as mere junk. "Before, everything on the molecular level was considered random. But there's actually selection going on at the molecular level, driving evolution on the organismic level. Because these mechanisms are being driven from the inside, that speeds the whole thing up." ☐

A transposon found only in humans may explain why we're so different from chimps

into new combinations. And, fortunately for us, RAG seems to have lost the ability to reinsert itself at random locations in the genome.

Transposons not only provide fodder for new genes, but they also have the power to shape organisms by influencing the intricate regulation of genes. Within the genome are enhancers and promoters—special sequences that switch genes on and off in different tissues. Transposons, too, are equipped with their own enhancers and promoters, and that can make them powerful players in evolution. "When transposons move around the genome and insert themselves near genes, they bring pre-evolved regulatory units with them, and that is prone to have a regulatory effect on nearby genes," explains McDonald.

In fact, Cal Tech molecular biologist Roy Britten, who was one of the first to spot transposons in the genomes of mammals, argues that the