JUMPING GENES:
How They Drove Primate Evolution

BY KEITH OLIVER & WAYNE GREENE

Jumping genes have been important in the evolution of higher primates, leading to faster brain function, improved foetal nourishment, useful red-green colour discrimination and greater resistance to disease-causing microbes – and even the loss of fat storage genes in gibbons.

Most DNA is inert, but some DNA sequences are mobile – they can move, or jump, from one location in a genome to another by copy and paste processes. These so-called transposable elements, or "jumping genes", are important because their activity within genomes gives them the *ability* to cause a great variety of genetic changes. While this can be harmful to the occasional individual, for example by causing a genetic disorder, overall it is a boon for the evolution of living things because it increases the amount of potentially beneficial genetic variation upon which natural selection can act. Jumping genes are thus not unlike Rumpelstiltskin, the fairy-tale rascal who was somewhat troublesome yet had the wondrous ability to spin straw into gold.

Jumping genes are ancient and ubiquitous, and are found throughout the animal and plant kingdoms. Long regarded as "junk DNA" by some, they can act over and above other known ways by which DNA mutations occur to make genomes more changeable, thereby boosting their evolutionary potential.

We have recently developed a hypothesis that explains how jumping genes provide an extra "evolutionary boost". According to the "transposon thrust" hypothesis, jumping genes powerfully promote evolution in one of two major ways.

1. In what we call active transposon thrust, jumping genes make changes to genomes through insertion into new locations or by inadvertently copying and pasting normal cellular genes from one place to another.
2. In passive transposon thrust, following insertion in multiple locations, jumping genes create a profusion of identical DNA sequences – a virtual "hall of mirrors" – that confuse the cellular machinery involved in DNA propagation, leading to an increased rate of duplications, deletions and reorganisations of chromosomal regions.

Through both of these ways, jumping genes can cause substantial and elaborate changes to genomes by creating new genes or altering the control of existing ones. This results in biological lineages that can adapt well to environmental changes or challenges and/or take advantage of new ecological opportunities. It can also pave the way for spectacular radiations of species and the generation of wholly new lineages. By this same reasoning, lineages lacking jumping genes can become "frozen" in evolution, possibly becoming "living fossils" or even extinct.

The activity and types of jumping genes present within genomes varies from lineage to lineage and also over time within any particular lineage. Their activity is usually intermittent, with periodic bursts of copy-and-paste activity due to either a relaxation of cellular controls (such as after stress), the emergence of new or modified jumping genes within a genome, or their transfer across species. Given enough time, most jumping genes suffer random mutations and eventually become incapable of activity.

Episodic jumping gene activity, and inactivity, helps to explain variations in the rate of evolution over time, why evolution appears to have stalled in some organisms, and why some lineages are highly successful and/or rich in species.

A key element of our transposon thrust hypothesis is that jumping genes can promote the origin of new lineages and subsequently exert a large influence on the course and extent of evolution within such lineages (see box, p.20).

The evolutionary history of primates is a case in point. Periodic bursts of jumping gene activity correlate with major divergence points in primate evolution, including splits between the higher primates and prosimians, the Old and New World monkeys and the apes and Old World monkeys. Over millions of years, the activity of jumping genes was such that, incredibly, they now make up nearly half (45%) of our entire genome!

Jumping gene activity is presently much reduced in primates, although higher primate genomes remain well-suited for passive transposon thrust, with just two types of jumping gene, the so-called *Alu* and *L1* repeats, predominating. These two elements have been amazingly prolific and now number a whopping 1.1 million and 516,000 copies, respectively, within the human genome.

The *Alu* jumping gene is particularly interesting. Not only is it extremely abundant, but it is only found in primates and cannot "jump" of its own accord. Instead it depends on the copy-and-paste machinery of *L1*.

Among other things, the higher primates have undergone significant advancements in brain function, reproduction and defence against infectious diseases. One can find some of the strongest specific evidence for the existence of transposon thrust by examining the evolution of the primate lineage.

Jumping genes have helped drive the separation of the higher primates away from the prosimians, or lesser primates, by engineering changes to DNA sequences that underpin many characteristics of monkeys, apes and/or humans. The advancement and radiation of higher primates seems to be, at least in part, due to exceptionally powerful transposon thrust, owing especially to the *Alu* element along with its *L1* partner. This evolutionary boost has operated in a variety of ways, most notably by:

- actively changing the control of pre-existing genes;
- actively changing the structure of pre-existing genes or creating entirely new genes;
- actively using the copy-and-paste mechanism to copy or destroy pre-existing genes; or
- passively acting as scattered near identical sequences (a "hall of mirrors") to cause duplications, deletions or reorganisations of chromosomal regions.

Actively Changing the Control of Pre-existing Genes

After inserting near a pre-existing gene, jumping genes can be very good at acting as control switches to turn genes on or off. Indeed, when Barbara McClintock first discovered jumping genes in the late 1940s, she called them "controlling elements".

Not surprisingly, this is a very major way by which jumping genes have influenced primate evolution. For example, the enzyme amylase, which digests starch, is produced in saliva (in

addition to the pancreas) in Old World primates (including humans) because long ago a jumping gene added a switch near the amylase gene that specifically works in the salivary gland.

Similarly, in a primate ancestor an *Alu* element pasted a switch near a gene called *FUT1* that allowed it to be turned on in red blood cells. The result was the ABO blood group system found only in apes and humans.

Such a mechanism has also helped in our immune defence against microbial invaders. For example, insertion of an *Alu* next to an antimicrobial gene called *CAMP* enabled this gene to be switched on by Vitamin D. Thus, in response to sunlight, the immune response of higher primates has been given a boost against infection.

Actively Changing the Structure of Pre-existing Genes or Creating Entirely New Genes

Jumping genes can contribute to the DNA sequences of genes themselves to create new functions. This appears to have happened many times in primate evolution, although the reason for the changes has, in most cases, not yet been determined.

Less commonly, but more spectacularly, jumping genes can provide the raw material to create entirely new genes from scratch. Two primate genes that are entirely derived from jumping genes are *Syncytin 1* and *Syncytin 2*, which play a crucial role in the formation of the higher primate placenta to help ensure a good connection between the mother and foetus.

Actively Using the Copy-and-Paste Mechanism to Copy or Destroy Pre-existing Genes

Certain jumping genes, such as *L1*, can actively create genetic novelties by using their copy-and-paste mechanism to partially or fully copy a pre-existing gene. The duplication of genes is a very important aspect of evolution as it creates spare copies of genes that can be tinkered with through further mutations. The result can be a new gene with a related but distinct function that may be beneficial to the survival and/or reproduction of its host, and thus be retained in evolution.

A good example of this in primates was the creation of the *GLUD2* gene from a copy of *GLUD1* following jumping gene activity. Only found in the most intelligent of primates (the apes and humans), *GLUD2* is specifically switched on in the brain, where it appears to speed up the recycling of the signalling chemical glutamate and hence improve learning and memory.

Of course, jumping genes can also be destructive when they insert into new locations in the genome. This is not always a bad thing, though, an example being the destruction of the *CMAH* gene by a jumping *Alu* sequence in a human ancestor about two million years ago. It is for this reason that humans lack a particular sialic acid molecule on the surface of their cells. The loss of *CMAH* probably conferred a survival advantage on the human lineage by decreasing the infectious risk from disease-causing microbes that use this molecule to attack cells.

Passively Acting as a "Hall of Mirrors" to Cause Duplications, Deletions or Reorganisations of Chromosomal Regions

When a single kind of jumping gene is present in very high numbers within a genome it can increase the chance of gain, loss or gross rearrangement of DNA by confusing the cell division machinery. In primates, the highly abundant *Alu* jumping gene, and to a lesser extent *L1*, have been particularly important factors in this process. For example, they have generated "carbon copies" of existing genes that have subsequently evolved distinct functions through point changes to their DNA sequences.

A very good example of this was the evolution of red-green colour vision in the Old World primate lineage, which includes apes and humans. Most mammals, including the prosimian primates, have colour-limited vision because they possess just

METHODS OF TRANSPOSON THRUST

Four main modes of transposon thrust explain the different modes of evolution apparent from the fossil record.

Mode 1: Active Thrust Only

Periodically active but highly mixed populations of jumping genes could lead to alternating periods of relatively fast evolution followed by little or no change. Active transposon thrust would come into effect during periods of jumping gene activity while there would be little or no passive transposon thrust due to the mixed bag of elements present.

Mode 2: Active and Passive Thrust

Periodically active and highly uniform large populations of jumping genes could lead to alternating periods of relatively fast evolution followed by more gradual change. Active transposon thrust would come into effect during periods of jumping gene activity while in between there may still be gradual change facilitated by passive transposon thrust due to the plethora of identical elements present.

Mode 3: Neither Active Nor Passive Thrust

Inactive and highly mixed populations of jumping genes could result in prolonged periods of little or no change, which may lead to eventual extinction and/or the occurrence of living fossils - notable examples being the tuatara and coelacanth. In this situation there is a lack of both active and passive transposon thrust.

Mode 4: Passive Thrust Only

Inactive and highly uniform large populations of jumping genes could result in long periods of gradual change. In this situation there is a lack of active transposon thrust, but there would still be ongoing passive transposon thrust.

two retina cone photoreceptor genes, one maximally sensitive to blue light and the other to green. The red–green perception trait apparently had its origin about 40 million years ago from a gene duplication event caused by *Alu* jumping gene sequences. This resulted in three retina cone photoreceptors, with the extra one becoming most sensitive to red light. Among other things, this beneficial change would have immensely improved the ability of the Old World primate lineage to find fruits and other foods.

Periodic bursts of jumping gene activity correlate with major divergence points in primate evolution...

A major focus during primate evolution was changes to reproductive physiology, with the higher primate placenta having developed a number of refinements to ensure efficient nourishment of the growing foetus. Here again, working in a passive manner, jumping genes appear to have played a key role.

For example, the growth hormone gene underwent a burst of duplications due to *Alu* sequences, with higher primates now possessing between five and eight copies of the gene. Many of these copies are switched on specifically in the placenta, where they help the foetus to acquire resources from the mother by influencing her metabolism.

In a similar fashion, one of the genes coding for haemoglobin, *HBG*, was duplicated in higher primates by the *L1* jumping gene to generate *HBG1* and *HBG2*. *HBG2* subsequently became switched on specifically in the developing foetus, where it ensures the high oxygen affinity of foetal blood for more efficient oxygen transfer across the placenta. Thus, the important process of gas exchange in the womb has been significantly improved by jumping genes in higher primates, in contrast to many other mammals, including prosimians, where foetal and adult haemoglobins are the same.

An interesting example of passive gene loss caused by jumping genes was the deletion of 100,000 base pairs of DNA specifically in the gibbon lineage of primates. The culprit behind this genetic mix-up was, yet again, the *Alu* sequence, and among the genes lost was *ASIP*, which promotes the storage of body fat. This may help to explain the wiry build of gibbons, which is so beneficial to their highly active life in the treetops.

Conclusion

A role for jumping genes in evolution has now been recognised by many, yet their importance has often been underestimated. Using primates as an example, the available evidence suggests that jumping genes, via transposon thrust, have played an instrumental role in engineering characteristic primate traits and thus have strongly contributed to the divergence of the higher primate lineage away from other types of mammal, including prosimians.

The beneficial features provided by jumping genes in the higher primates include faster brain function, improved foetal nourishment, useful red-green colour discrimination and greater resistance to disease-causing microbes. Such large evolutionary benefits powerfully demonstrate that if jumping genes are "junk DNA" then there is indeed much treasure to be found in the junkyard.

Keith Oliver is a biologist and philosopher in the School of Biological Sciences and Biotechnology and Wayne Greene is Associate Professor of Molecular Genetics in the School of Veterinary and Biomedical Sciences at Murdoch University.