The design of life: part 4—variation-inducing genetic elements and their function

Peter Borger

Endogenous retroviruses (ERVs) are believed to be the selfish remnants of ancient RNA viruses that invaded the cells of organisms millions of years ago and now merely free-ride the genome in order to be replicated. This selfish gene thinking still dominates the public scene, but well-informed biologists know that the view among researchers is rapidly changing. Increasingly, ancient RNA viruses and their remnants are being thought of as having played (and still do) a significant role in protein evolution, gene structure, and transcriptional regulation. As argued in part 3 of this series of articles, ERVs may be the executors of genetic variation, and qualify as specifically designed variation-inducing genetic elements (VIGEs) responsible for variation in higher organisms. VIGEs induce variation by duplication, transposition, and may even rearrange chromosomes. This extraordinary claim requires extraordinary scientific support, which is present throughout this paper. In addition, the VIGE hypothesis may be a framework to understand the origin of diseases and explain rapid speciation events through facilitated chromosome swapping.

The idea that mobile genetic elements are involved in creating variation is not new. Barbara McClintock, who discovered the first mobile genetic elements in maize, was also the first to recognize the true nature of such jumping genetic elements. In 1956, she suggested that transposons (as she coined them) function as molecular switches that could help determine when nearby genes turn on and off. Her key insight was that all living systems have mechanisms available to restructure and repair the chromosomes. When it was discovered that more than half of the human genome consists of (remnants of) mobile elements, McClintock's ideas were revived and further developed by Roy Britten and Eric Davidson.[1] It is only recently that we have begun to understand the power of VIGEs (variation-inducing genetic elements) as genetic regulators and switches. A team of investigators lead by Haussler recently provided direct evidence that even when a short interspersed nucleotide element (SINE) lands at some distance from a gene, it can take on a regulatory role with powerful regulatory functions.[2]

> 'Haussler and his colleagues then looked at a particular example—a copy of the ultra-conserved element that is near a gene called Islet 1 (ISL1). ISL1 produces a protein that helps control the growth and differentiation of motor neurons. In the laboratory of Edward Rubin at the University of California, Berkeley, postdoctoral fellow Nadav Ahituv combined the human version of the LF-SINE sequence with a "reporter" gene that would produce an easily recognizable protein if the LF-SINE were serving as its on-off switch. He then injected the resulting DNA into the nuclei of fertilized mouse eggs. Eleven days later, he examined the mouse embryos to see whether and where the reporter gene was switched on. Sure enough, the gene was active in the embryos' developing nervous systems, as would be expected if the LF-SINE copy were regulating the activity of ISL1.'[3]

This excerpt shows that some functions of SINEs are easily uncovered because they are directly affecting the expression of a particular gene. However, most functions of SINEs may not be as easily detected as described of above, because they can integrate in *gene deserts*—regions of the genome where the chromosomes are devoid of any recognizable protein-coding genes—or they may only subtly affect expression of morphogenetic programs. Gene expression patterns largely determine how cells behave and determine the morphology of organisms. VIGEs integrated in such genetic programs will change expression patterns of genes that will result in different cellular behaviour and morphology. Whether the ultimate effect on the phenotype of the organism can be predicted, however, remains to be established. This is largely due to the fact that we still do not know what morphogenetic algorithms look like. Of course, biologists have argued that evolution and development are determined by homeobox (HOX) genes, but HOX genes are merely executors of developmental (or morphogenetic) programs; they are not the programs themselves.

In another study by the same group, thousands of short identical DNA sequences that are scattered throughout the human genome were analyzed. Many of those sequences were located in gene deserts, which are in fact so clogged with regulatory DNA elements that they have recently been renamed *regulatory jungles*. But what do they regulate? The answer could be morphogenesis. Most of the short DNA elements cluster near genes that play a decisive role

during an organism's first weeks after conception. The elements help to orchestrate an intricate choreography of 'when-and-where' developmental genes are switched on and off as the organism lays out its body plan. These elements may provide a sort of blueprint for how to build the animal. The exact mechanism as to how such sequences may function as a plan to build an animal is not entirely clear, but the DNA elements are particularly abundant near genes that help cells to stick together. That 'stickiness' is important in an organism's early life phase because these genes help cells to migrate to the right location and to form into organs and tissues of the correct shape. The 10,402 short DNA sequences studied by Bejerano are derived from transposable genetic elements—retrotransposons that duplicate themselves and hop around the genome. Apparently, transposable genetic elements are not what they have been mistakenly thought to be: mess makers. Indeed, the view that transposable elements are just bad stuff is rapidly changing. In an interview with Science Daily, Bejenaro says:

> 'We used to think they were mostly messing things up. Here is a case where they are actually useful.'[4]

The genome is literally littered with thousands of transposable elements. The word is that 'when ancient retroviruses slipped bits of their DNA into the primate genome millions of years ago, they successfully preserved their own genetic legacy.'[5] It is hard to imagine that they all have functions, but their presence could certainly determine or fine-tune the output of nearby genes. In this way they may create subtle, but novel, variation. Bejenaro and Haussler's research has already identified a handful of transposons that serve as regulatory elements, but it is not clear how common the phenomenon might be. The 2007 study showed that the phenomenon may be a general one:

> 'Now we've shown that transposons may be a major vehicle for evolutionary novelty.'[4]

The new findings indeed show that, in many cases, transposable elements function as regulators of gene output, but major vehicles for evolution from microbe to man they are not. The transposition of jumping genetic elements may certainly affect gene expression patterns, but it does not follow that they produce new genetic information. Considering the biological data, it seems reasonable that transposable elements are present in the genome to *deliberately induce biological variation*. Transposable elements thus qualify as *variation-inducing genetic elements* (VIGEs), and by leaving copies, they make sure the new variation is heritable. The transposable elements present in regulatory jungles do not produce new biological information, but they induce variation in the genetic algorithms and may underlie rapid adaptive radiation from uncommitted pluripotent genomes. The regulatory jungles may provide an active reservoir of VIGEs that put existing genes in new regulatory environments.

Regulated activity of VIGEs

The chromosome of the *E. coli* strain K12 includes three cryptic operons (linear genetic programs that encode programs to metabolize three alternative sugars): one for cellobiose, one for arbutin and one for salicin. The organization of those operons is like a normal substrate-induced bacterial operon; but the operons themselves are abnormal in that they are cryptic (silent) in wild-type strains. Even in the presence of alternative sugars the operons are not activated, which indicates that these bacteria don't readily use alternative sugars. Unused cryptic operons are redundant genetic programs that are not observed by natural selection:

> 'As cryptic genes are not expressed to make any positive contribution to the fitness of the organism, it is expected that they would eventually be lost due to the accumulation of inactivating mutations. … Cryptic genes would thus be expected to be rare in natural populations. This, however, is not the case. Over 90% of natural isolates of *E. coli* carry cryptic genes for the utilization of beta-glucoside sugars. … These cryptic operons can all be activated by IS [insertion-sequence] elements, and when so activated allow *E. coli* to utilize beta-glucoside sugars as sole carbon and energy sources.'[6]

The excerpt shows that operons are kept inactive by repressors; that is, proteins that sit on the DNA of the operon to ward off the nanomachines responsible for gene expression. Operons will only be active in bacteria that don't have a functional gene coding for the repressors. Disrupting the repressor gene releases the cryptic programs. That's where the VIGEs come in. The transposition and integration of an IS element into the silencer elements is the mutational event that activates the cryptic operon. Usually, the lack of an appropriate carbon and energy source triggers transposition of IS elements. The transposition of IS elements appears to be regulated by starvation, and the integration in the repressor gene is not utterly random. For instance, position 472 in the *ebgR* gene in the ebg operon of *E. coli* is a hotspot for integration of IS elements, but only under starvation conditions. VIGEs may thus accumulate and integrate at well-defined positions in the genome; this indicates a site-specific mechanism.

In the fruit fly, some non-LTR (long terminal repeats retrotransposons) integrate at very specific sites, but some others have been shown to integrate more or less at random. The specificity is determined by endonucleases, enzymes that cut the DNA.[7] Assuming VIGEs are part of a designed genome, we must expect that their transposition and activity can be controlled and regulated. To avoid deleterious effects on the host and retrotransposon, we may expect that the activity of VIGEs is regulated both by retrotransposon- and host-encoded factors. Indeed, the mechanism of transposition seems to be dictated by the

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Human         TGCCAATAGAGATAGAAAGAATGGATGGAACAGACATGCATTTAAGAAGGTTCA<Alu>AAGAAGGTTCAGCAGAGTGTGGTGAAGACTGGGC
Chimpanzee    TGCCAATAGAGATAGAAAGAATGGATGGAACAGACATGCATTTAAGAAGGTTCA----------------GCAGAGTGTGGTGAAGACTGGGC
Gorilla       TGCCAATAGAGATAGAAAGAATGGATGGAACAGACATGCATTTAAGAAGGTTCA<Alu>AAGAAGGTTCAGCAGAGTGTGGTGAAGACTGGGC
Orangutan     TGCCAATAGAGATAGAAAGAATGGATGGAACAGACATGCATTTAAGAAGGTTCA<Alu>AAGAAGGTTCAGCAGAGTGTGGTGAAGACTGGGC
Owl Monkey    TGCCAATAGAGAGAGAAAGAATGGATGGAACAGACATGGATTTAAGAAGGTTCA----------------GCAGAGTGTGGTGAAGACTGGGC
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Figure 1. The Alu HS6 insertion sites in human, chimpanzee, gorilla, orangutan and owl monkey. Note the complete absence in chimpanzee and owl monkey of any evidence for an extraction site. This suggests a highly specific mechanism for integration and/or extraction. Otherwise, the sequences are a molecular falsification of the common descent of primates.

species in which the VIGEs operate. Recent research has shown that in zebra fish the transposable element known as *NLR integrant* usually carries a few extra nucleotides at the far end of the sequence, but it is not expressed in human cells.[8] This observation would argue for the involvement of host specific protein machinery in transposition—one more argument for the design origin of VIGEs.

From the design perspective, we may expect that the activity of VIGEs used to be a tightly controlled process. This is because the genomes in which they operate also specify control factors: retroviral restriction factors. The restriction factors are proteins with the ability to bind to retroviral capsid proteins and target them for degradation. Several restriction factors have been identified, including Fv1, Trim5alpha and Trim5-CypA.[9] These factors share the common property of containing sequences that promote self-association: that is, they can assemble themselves. This fact, together with the observation that the restriction factors are encoded by unrelated genes, is clear evidence of purposeful design. Retroviral restriction factors play an important role in innate immunity against invading RNA viruses. For instance, Trim-5alpha binds directly to the incoming retroviral capsid core and targets its premature disassembly or destruction.[10] In addition, some integrated VIGEs show evolutionary-tree deviations, indicating a sequence-specific integration/excision mechanism. For instance, *Alu HS6* is present in human, gorilla and orangutan, but not in chimpanzee (see figure 1). This highly peculiar observation prompted the investigators to consider the possibility of the specific excision of this *Alu* element from the chimpanzee's genome.[11] Precise excision implies precise integration.

Biologists specializing in synthetics at the Johns Hopkins University have built, from scratch, a LINE1-based retrotransposon—a genetic element capable of jumping around in the mouse genome. The man-made retrotransposon was designed to be a far more effective 'jumper' than natural retrotransposons; indeed, it inserts itself into many more places in the genome.[12,13] Why do not all LINEs jump so effectively? The scientists that constructed the synthetic LINE changed the regulator sites used in transposition. Native LINE1 elements are relatively inactive in mice when they are introduced into the mouse genome as transgenes. The synthetic LINE1-based element, ORFeus, contains two synonymously recoded ORFs relative to mouse L1 and is far more active. This indicates that the integration and excision of native LINE1 elements are controlled and regulated by an as yet unknown mechanism.

VIGEs qualify as redundant genetic elements that can simply be erased from the genome without fitness effects. As long as VIGEs do not upset critical genomic functions and do affect reproductive success of the carrier, they are selectively neutral. Therefore, not only VIGEs, but also the mechanisms by which they integrate, may readily wither and degrade due to accumulation of debilitating mutations. The control over integration and activity we observe today may be less stringent compared to how it was originally designed. The originally fine-tuned control for excision and transposition may have deteriorated over time and what is left today are more or less free moving elements that may predominantly cause havoc when they integrate in the wrong location. It is easy to understand how, for instance, endonucleases became less specific through mutations. This view may also explain why VIGEs are often found associated with heritable diseases. As long as VIGE activity and integration do not significantly affect the fitness of the organisms in which they operate, they are free to copy and paste themselves along the genome. Indeed, inactivating VIGEs have been observed in genes not immediately required for reproduction. The GULO gene, which qualifies as a redundant gene in populations with high vitamin C intake, has been hit several times by VIGEs and this may have contributed to pseudogenization of GULO in humans.[14]

Over time, VIGEs may have become increasingly detrimental to the host's genome. That is because information that regulates the integration and activity of VIGEs is subject to mutation. Some VIGEs have been associated with susceptibility or resistance to diseases. In asthma, increased susceptibility appears to be associated with microsatellite DNA instability (a term used for copy-number differences in repetitive DNA sequences).[15] Psoriasis is also associated with HERV expression.[16] It should be clear that deregulated and uncontrolled VIGEs cause havoc when they integrate with and disrupt functional parts of genes.

From the vantage of design, VIGE transpositions would make sense during meiosis, which is the process leading to the formation of gametes. Controlled activity of VIGEs

during meiosis may be responsible for variation that can be passed on to the offspring. Although information is scant, it has been shown in fungi[17] and plants[18] that VIGEs become active during meiosis and even have mechanisms to silence deleterious bystander-effects, such as deleterious point mutations.[17] This shows transposable elements function to induce genetic variation, providing the flexibility for populations to adapt successfully to environmental challenges. In chimpanzees, for instance, it has been documented that large blocks of compound repetitive DNA, which have demonstrated retrotransposon function, induce and prolong the bouquet stage in meiotic prophase and affect chiasm formations.[19] This may seem like a mouthful, but it merely means that these repetitive genetic elements facilitate sister-chromosome exchanges when reproductive cells (sperm and eggs) are being generated. Mammalian VIGEs, in particular Alu sequences, have the ability to induce genetic recombination and duplications and contribute to chromosomal rearrangements, and they may account for the major part of variation observed in humans. The methylation pattern of Alu sequences possibly determine activity and/or serve as markers for genomic imprinting or in maintaining differences in male and female meiosis. [21]

VIGEs and the human family

When short triplet repeat units are present in the coding part of a gene, they may even have functional consequences. There is evidence that repeat units in the *Runx2* gene formed the bent snout of the Bullterrier in a few generations.[22] Likewise, in mice and dogs, having five or six toes is determined by a repeat unit in the *Alx4* gene.[23] These novel phenotypes can form almost over night, i.e. within one generation. Repetitive coding triplets that can be gained or lost provide another mechanism to generate (instant) variation. It should be noted that this mechanism leads to reversible genetic change, because a lost repetitive unit can readily be added back through duplication of a preexisting one, and vice versa. Therefore, the RTS mechanism may explain seasonal changes in beak size observed for Galapagos finches, adaptive phenotypes in Australian snakes and the 'evolution' of the Cichlid varieties in African lakes.

If we accept the idea of deliberately designed VIGEs, we may also expect these elements to have played an important role in determining the variety of human phenotypes. In other words, human races are the result of the activity of VIGEs! Biologists used to think that our genomes all had the same basic structure—the same number of genes, in roughly the same order, with a few minor differences in the sequence of DNA bases. Now, technologies that compare whole human genomes are revealing that this picture is far from complete. Michael Wigler at Cold Spring Harbor Laboratory provided the first evidence that human genomes are strikingly variable: his group showed marked differences in the copy number of protein-coding genes.[24] Apparently, some people have more copies of certain genes and, large-scale copy number polymorphisms (CNPs) (about 100 kilobases and greater) contribute substantially to genomic variation between individuals.[25] In addition, people not only carry different copy numbers of parts of our DNA they also have varying numbers of deletions, insertions and other major rearrangements in their genomes.

In 2005, Evan Eichler of the University of Washington reported 297 locations in the genome where different individuals have different forms of major structural variations. At these spots some carry a major deletion, for example, or an extra hundred bases of DNA. Differences between individuals were found in the protein-coding genes; structural differences were also observed between individual genomes.[26] From these and other studies we now know that every one of us shares only about 99% of our DNA with all the other people on Earth.[27] The difference is due to repetitive sequences that easily amplify or delete parts from the genome. With this, we have discovered another class of VIGEs. The highly variable repetitive sequences also explain why genetic screening methods are so reliable nowadays: they detect copy-number differences and hence are capable of discriminating between the DNA of a father and his son. Yes, fathers and sons apparently differ at the level of VIGEs!

A comparison of Asian and Caucasian people showed that 25% of more than 4,000 protein-coding genes had significantly different expression patterns. Some gene expression levels differed as much as twofold.[28] The researchers commented that these findings 'support … the idea that there are genetically determined characteristics that tend to be clustered in different ethnic groups.' Some genes are simply not expressed at all, or are simply not present in the genomes. For instance, the gene *UGT2B17* is deleted more often in Asians than in Caucasians, and has a mean expression level that was more than 20 times greater in Caucasians relative to Asians. How can such big differences be explained? Of course, single nucleotide polymorphisms (SNP; i.e. point mutations) in regulatory sequences could affect gene regulation patterns. It is not clear, however, 'whether the SNPs themselves might be regulating gene expression or whether they travel together with other DNA that's the regulator.' We may also expect VIGEs to be responsible for differences observed between human races.

VIGEs and chromosome 2

Human chromosome 2 looks as if it is the product of the fusion of two chromosomes that we find in chimpanzees as chromosome 12 and 13. Therefore, some Darwinists take human chromosome 2 as the ultimate evidence for common descent with chimpanzees. We *know* that a fusion of two ancestral chromosomes would have produced human chromosome 2 with two centromeres. Currently, human chromosome 2 has only one centromere, so there

must be molecular evidence for remnants of the other. In 1982, Yunis and Prakash studied the putative fusion site of chromosome 2 with a technique known as fluorescence *in situ* hybridization (FISH) and reported *signs* of the expected centromere.[29] In 1991, another study also reported *signs* of the centromere.[30] In 2005, after the complete sequencing of human chromosome 2, we would have expected full proof of the ancestor's centromere. However, even after intense scrutiny there are still only *signs* of the centromere. If signs of the centromere were already observed in 1982, why can it not be proved in the 2005 sequence analysis? Apparently, the site mutated at such high speed it is no longer recognizable as a centromere:

> 'During the formation of human chromosome 2, one of the two centromeres became inactivated (2q21, which corresponds to the centromere of chromosome 13) and the centromeric structure quickly deteriorated'.[31]

Why would it quickly deteriorate? Why would this region deteriorate faster than neutral? A close up scrutiny in 2005 showed the region that has been interpreted as the ancestor's centromere to be built from sequences present in 10 additional human chromosomes (1, 7, 9, 10, 13, 14, 15, 18, 21 and 22) as well as a variety of other genetic repeat elements that were already in place before the fusion occurred.[33] The sequences interpreted as 'ancient centromere' are merely repetitive sequences and may actually qualify as (deregulated) VIGEs.

The chimpanzee and human genome projects demonstrated that the fusion did not result in loss of protein coding genes. Instead, the human locus contains approximately 150,000 additional base pairs not found in chimpanzee chromosome 12 and 13 (now also known as 2A and 2B). This is remarkable: why would a fusion result in *more* DNA? We would rather have expected the opposite: the fusion would have left the fused product with less DNA, since loss of DNA sequences is easily explained. The fact that humans have a unique 150 kb intervening sequence indicates it may have been deliberately planned (or designed) into the human genome. It could also be proposed that the 150 kb DNA sequence demarcating the fusion site may have served as a particular kind of VIGE, an adaptor sequence for bringing the chromosomes together and facilitating the fusion in humans.

Another remarkable observation is that in the fusion region we find an inactivated cobalamin synthetase (CBWD) gene.[32] Cobalamin synthetase is a protein that, in its active form, has the ability to synthesize vitamin B12 (a crucial cofactor in the biosynthesis of nucleotides, the building blocks of DNA and RNA molecules). Deficiency during pregnancy and/or early childhood results in severe neurological defects because of impaired development of the brain. The Darwinian assumption is that the cobalamin synthetase gene was donated by bacteria a long time ago and afterwards it was inactivated. Nowadays, humans must rely on microorganisms in the colon as well as dietary intake (a substantial part coming from meat and milk products) for their vitamin B12 supply. It is also noteworthy that humans have several copies of inactivated cobalamin-synthetase-like genes on a number of locations in the genome, whereas chimpanzees only have one inactivated cobalamin synthetase gene. That the fusion must have occurred after man and chimp 'split' is evident from the fact that the fusion is unique to humans:

> 'Because the fused chromosome is unique to humans and is fixed, the fusion must have occurred after the human-chimpanzee split, but before modern humans spread around the world, that is, between 6 and 1 million years ago.'[34]

The molecular analyses show we are more unique than we ever thought we were, and this is in complete accordance with creation. Apparently the fusion of two human chromosomes that took place may have been the result of an intricate rearrangement or activation of repetitive genetic elements after the Fall (as part of, or executors of, the curse following the Fall) and inactivated the cobalamin synthetase gene. The inactivation of the gene may have reduced people's longevity in a similar way as the inactivation of the GULO gene, which is crucial to vitamin C synthesis.[14] Understanding the molecular properties of human chromosome 2 is no longer problematic if we simply accept that humans, like the great apes, were originally created with 48 chromosomes. Two of them fused to form chromosome 2 when mankind went through a severe bottleneck.[33] And, as argued above, the fusion was mediated by VIGEs.

The upside-down world

The p53 protein is a mammalian transcription factor that functions as the main switch controlling whether cells divide or go into apoptosis (programmed cell death, which is sometimes required for severely damaged cells that may become tumours). Scientists have long wondered how p53 gained the ability to turn on and off more than 1200 genes related to cell division, DNA repair and programmed cell death. Without the p53 control system organisms would not function: all life would have died as bulky tumors.

Biologists at the University of California now claim that ancient retroviruses helped p53 to become an important master gene regulator in primates.[34] An RNA virus invaded the genome of our common ancestor, jumped into hundreds of new positions throughout the human genome and spread numerous copies of repetitive DNA sequences that allowed p53 to regulate many other genes, the team contends. Studies such as these prompted Darwinians to change their minds about jumping genetic elements. In other words, a randomly hopping ERV provided the human genome with carefully regulated decision-making machinery. The idea is beyond reasonable belief. Darwinists tend to mix things up. What really happened in the human genome is a

read-through of polymerase II in a VIGE that was next to a gene that already contained a binding site for p53. Or maybe the VIGE was excised improperly, taking a bit of a flanking gene containing the p53 binding site. Next, the modified VIGE amplified, transposed, amplified and so on. That explains this family of transposons. A similar story can be told for the syncytin gene, which encodes a protein of the mammalian placenta that helps the fertilized egg to become embedded in the uterus wall. Since syncytin has also been found on a transposable element,[35] mammals are alleged to have obtained the gene from an RNA virus that infected a mammalian ancestor millions of years ago. It is more likely, however, that syncytin was captured by a VIGE.

In bacteria it is often observed that genes that convey a specific advantageous character are transmitted via plasmids. Plasmids often contain genes for alternative metabolic routes or genes that provide resistance to antibiotics, and they replicate independently from the host's genome. Plasmids easily shuttle between microorganisms via a DNA uptake-process known as transformation (or horizontal gene transfer). The uptake of plasmids is regulated and controlled, and is DNA sequence dependent. The result of DNA transformations is rapid adaptation to, for instance, antibiotics. Likewise, viruses replicate independently from the genomic DNA, leaving many copies and easily transferring from one organism to another. Viruses are not plasmids, although some viruses may have a similar function in higher organisms as do plasmids in bacteria: they may be able to aid in rapid adaptations to changing environments. It has been observed that a virus can indeed transfer an adaptive phenotype. The virus that is present in the fungus *(Curvularia protuberata),* can induce heat resistance in tropical panic grass (*Dichanthelium lanuginosum*), allowing both organisms to grow at high soil temperatures in Yellowstone National Park. This shows that 'viruses' still provide strategies for rapid adaptation.

> 'Fungal isolates cured of the virus are unable to confer heat tolerance, but heat tolerance is restored

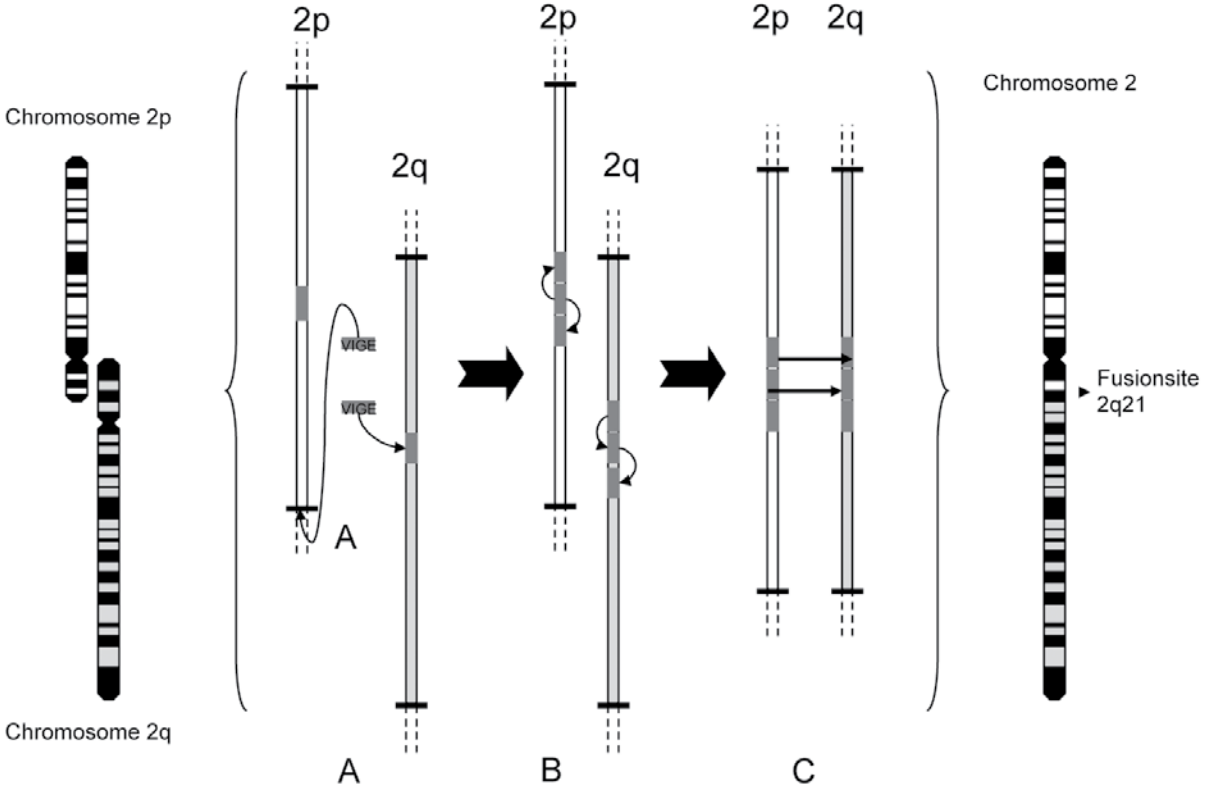

Figure 2. Putative mechanism how the human chromosome 2 formed through the fusion of two ancestral chromosomes p2 and q2, which are also known as chimpanzee chromosome 12 and 13). Like the great apes, originally the human baranome may have contained 48 chromosomes. **A)** Independent transposition events may have led to the integration of a relative small variation-inducing genetic element (VIGE). **B)** Extended duplication events of the VIGE may have resulted in rapid expansion of the region in both p2 and q2, preparing it to become an 'adapter sequence' required for fusion. **C)** The expanded homologous regions align and facilitate the fusion of the chromosomes. The fusion region (2q21) and other parts of the modern human genome still shows the remnants of this catastrophic event that only occurred in humans: the cobalamin synthetase gene was inactivated and several inactive copies, which are not found in the chimpanzee, scattered throughout the genome. Speculative note: Before the great flood, and probably shortly after, a balancing dynamics of both 48 and 46 chromosomes may have been present in the human family. This may explain the two extreme cranial morphologies present in the human fossil record. The *Homo erectus*/Neandertal humans may have had a karyotype comprised of 48 chromosomes (non-fused p2 and q2), whereas the other humans had 46 (fused p2 and q2).

after the virus is reintroduced. The virus-infected fungus confers heat tolerance not only to its native monocot host but also to a eudicot host, which suggests that the underlying mechanism involves pathways conserved between these two groups of plants.'[36]

In fruit flies, wing pigmentation depends on a gene known as *yellow*. The gene exists in the genome of all individual fruit flies, but in some it is not active. By analysing the genetic origin of the spots on fruit fly wings, researchers have discovered a molecular mechanism that explains how new patterns of pigmentation can emerge. The secret appears to be specific genetic elements that orchestrate where proteins are used in the construction of an insect's body. The segments do not code for proteins, but rather regulate the nearby gene that specifies the pigmentation. As such, these regulatory DNA segments qualify as VIGEs. The researchers transferred the regulatory DNA segment from a spotted species (*Drosophila biarmipes*) into another species not expressing the spot (*D. melanogaster*), and attached the regulatory region to a gene for a fluorescent protein. They found that the fluorescent gene was expressed in the spot-free species in exactly the same patterns as the yellow gene is expressed in the spotted species. By comparing several spotted and spotfree species, the scientists established that mutation of a regulatory DNA segment led to the expression of the spotted trait. They discovered that in the species with spotted wings this regulatory segment has *multiple binding sites* for a protein that then activates the *yellow* gene. Spotless species do not have multiple binding sites.[37] The multiplicity of regulatory DNA segments may argue for an amplification mechanism or targeted integration of the regulatory sequence. That explains why the same pattern of pigmentation can emerge independently in distantly related species (Darwin's analogous variation). The observed shuttle function of viruses leads me to pose an intriguing question: Were endogenous retroviruses originally designed to serve as shuttle-vectors to deliver messages from the soma to the germ-line? If yes, then it would put Lamarckian evolution in an entire new perspective.

Discussion

The findings of the new biology demonstrate that mainstream scientists are wrong regarding the idea that transposable elements are the selfish remnants of ancient invasions by RNA viruses. Instead, RNA viruses originate from transposable elements that were designed as variation-inducing genetic elements (VIGEs). Created kinds were deliberately frontloaded with several types of controlled and regulated transposable elements to allow them to rapidly invade and adapt to all corners and crevices of the earth. Due to the redundant character of VIGEs, their controlled regulation may have readily deteriorated and some of them may now merely cause havoc. The VIGE hypothesis provides elegant explanations for several biological observations that may otherwise be difficult to interpret within the creationist framework, including the origin of diseases (RNA viruses) and chromosome rearrangements. The VIGE hypothesis may be a framework for extended creationist research programs. Some intriguing question can already be raised.

1. *Were VIGEs intentionally designed to cause diseases?* No, they were not. It is conceivable that the transposition and integration of VIGEs is not entirely random. The transposition of VIGEs may have been originally present in the baranome as controlled and regulated elements and activated upon intrinsic or external triggers. To induce variation in offspring, triggers for the transposition of VIGEs could be released during meiosis, when the reproductive cells are being produced. The emergence of RNA viruses from VIGEs may be a result of the Fall, when we were cut of from the regenerating healing power of the Creator.
2. *Why are some VIGEs located on the exact same position in primates and humans?* Each original baranome must have had a limited number of VIGEs, some of which we still find on the same location in distinct species. In distinct baranomes, VIGEs may have been located on the exact same positions (the T-zero location), which then explains why some VIGEs such as ERVs, can be found in the same location in, for instance, primates and humans. In addition, sequence-dependent integration of VIGEs may also contribute to this observation.
3. *How could Bdelloid rotifers, a group of strictly asexually reproducing aquatic invertebrates, rapidly form novel species?* Asexual production of progeny, as observed in Bdelloids, is found in over one half of all eukaryotic phyla and is likely to contribute to adaptive changes, as suggested by recent evidence from both animals and plants.[38] The Bdelloids may have been derived from pluripotent baranomes containing numerous DNA transposons and retro elements, including active LTR retrotransposons containing *gag*, *pol*, and *env*-like open reading frames.[39] These elements are able to reshuffle the genomes and facilitate instant variation and speciation.
4. *Do we also observe remnants of DNA viruses in the mammalian genomes?* If not, this advocates my idea that RNA viruses emerged from VIGEs, and implies DNA viruses have a different origin; probably, as with the Mimi-virus[40], they originated from degenerated bacteria.
5. *Why was a class of VIGEs designed with information for protein capsids?* The capsid may have been acquired from the host's genome or it may have been designed to prevent the RNA molecules from attaching themselves to, or finding, integrations sites. A very speculative idea may be that these VIGEs were designed to shuttle information from the soma to the germ-line. One thing is clear, however: creation researchers have loads of work to do.

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Peter Borger has an M.Sc. in Biology (Honours biochemistry and molecular genetics) and a Ph.D. in Medical Sciences from the University of Groningen, The Netherlands. He is currently working on the cellular and molecular aspects of pulmonary diseases, such as asthma and COPD, and is an authority on the molecular biology of signal transduction and gene expression.