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Paper report

Poised for contagion: evolutionary origins of the infectious abilities of invertebrate retroviruses.

HS Malik, S Henikoff, TH Eickbush. *Genome Res* 2000, **10:** 1307-1318.

Invertebrate retroelements have borrowed diverse viral envelopes for infection

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Significance and context

Several groups of long-terminal repeat (LTR) retrotransposons have a third open reading frame (ORF) in addition to the *gag* and *pol* genes that are always present. These ORFs usually have structural features strikingly reminiscent of the genes for viral glycoproteins involved in host recognition and fusion of the virus envelope with host cell membranes, and so are a crucial determinant of virulence. The transposon genes have been named envelope genes (*env*) by analogy with these viral products, and the presence of this gene has long been recognized as the crucial difference between retrotransposons and retroviruses: in one case - the gypsy-related insect errantiviruses - the virus-like particles produced have been shown to be infective, demonstrating an evolutionary transition from retrotransposon to fully functional retrovirus. *Env*-like genes are known in retrotransposons from plants, insects and nematodes, and from all but one lineage of LTR retroelements (the exception being the DIRS1 clade, but only three examples of this group are known).

Much research has focused on the vertebrate retroviruses, where the Env proteins are important antigenic sites. Unfortunately, this involvement in mediating host immune responses produces strong selective pressure for polymorphism, producing rapid sequence divergence at this locus. It has therefore proved impossible to ascertain the origins of the *env* gene of these retroviruses. It is not even certain whether the vertebrate retroviruses acquired these genes in a single event or as multiple independent horizontal transfers. It has been established that the plant caulimoviruses, derived from a retrotransposon lineage, have cell-to-cell movement proteins related to those of a number of plant viruses. Now, Malik *et al.* present convincing evidence for the origins of the *env* genes of three distinct lineages of invertebrate retroviruses.

Key results

Database searches with a conserved block of amino acids from the divergent Env proteins of insect errantiviruses identified similarity to ORFs from some baculoviruses (a group of double-stranded DNA insect viruses). The baculoviral ORFs have the transmembrane regions and signal peptides expected of viral envelope proteins, and tend to occur in viruses lacking the described baculoviral 'envelope analogous' gp64 gene, suggesting that the identified ORFs represent a second, unrelated envelope protein of baculoviruses. The fact that the errantiviruses are derived from a lineage of retrotransposons, whereas all known baculoviruses are infectious, strongly suggests that these genes originally evolved in a baculoviral genome and have subsequently been acquired by the errantiviruses. Cer elements from *Caenorhabditis elegans* are members of the BEL clade of LTR retrotransposons, and contain *env* genes showing strong similarity to phlebovirus G2 glycoproteins, whereas the closely related Tas element from *Ascaris* shows some limited similarity to herpesvirus gB glycoprotein, the herpesvirus protein primarily implicated in infection. The low similarity between Tas and the herpesvirus sequences is possibly because Tas appears to be a dead 'pseudoelement', with multiple frameshifts and termination codons, and so could have diverged substantially from a functional sequence.

Conclusions

It appears that the transition from nonviral retrotransposon to retrovirus has occurred independently at least eight times, and the source of the envelope gene responsible for infectious ability can now be traced to a virus in at least four of these instances. This suggests that "potentially, any LTR retrotransposon can become a virus" through the acquisition of existing viral genes.

Reporter's comments

The results confirm that retrotransposons can routinely become virulent through the acquisition of existing viral genes. Presumably, the *env* genes displayed by the retroviral lineages discussed here have been acquired by the same mechanism as that involved in retroviral transduction of cellular oncogenes. This is thought to be an illegitimate recombination event involving the terminal repeats, presumably occurring during viral infection of a host cell. The fact that retrotransposons are known to have transferred across species, and that LTR retrotransposons have been found integrated into viral genomes, suggests that these elements could reach a new host and gain the molecular machinery necessary to infect that host in a single event. This new evidence that any retrotransposon is a potential 'retrovirus-in-waiting' should be sobering news to those working on xenotransplantation techniques.

It is exciting news for evolutionary biologists. Supporters of a 'strong adaptationist' view would expect that the various parts of a genome have closely coevolved to form a tightly integrated whole, particularly in a viral parasite with very short generation times and under strong selective pressure from a host immune response. If new retroviruses can get by as functional parasites with a newly acquired host invasion protein this suggests that these viruses are to some degree modular, with any replication machinery being able to work with any coat protein and any invasion system. More data on retroelements from genome sequencing projects, and more data on viral genomes themselves could make these tiniest of genomes important models of how different genes

interact to produce a functional system with a successful life history.

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