Science 10 August 2001:
Vol. 293. no. 5532, p. 1048
DOI: 10.1126/science.293.5532.1048a

LETTERS

Lateral Gene Transfer or Viral Colonization?

S. L. Salzberg and colleagues reexamined data that had been published by the international human genome sequencing group in which it appeared that between 113 and 223 genes were present in the human genome but were absent from lower eukaryotes (*Caenorhabditis elegans, Saccharomyces cerrevisiae, Drosophila melanogaster, Arabidopsis thaliana*) (Reports, "Microbial genes in the human genome: Lateral transfer or gene loss?", 8 Jun., p. 1903). This result had suggested that these genes had undergone direct bacterial-to-vertebrate transmission (lateral transfer). From their reevaluation of this set of genes and inclusion of genomes of additional eukaryotic parasites, Salzberg and colleagues conclude that many of these candidate transfer genes appear to have been lost from the original lower eukaryotic set and that gene loss is the more plausible explanation for this result. In an accompanying Perspective ("Are there bugs in our genome?", p. 1848), Jan O. Andersson and co-authors note that at least some of these genes (the *N*-acetylneuraminate lyase, for example) retain a phylogenetic pattern consistent with lateral transfer.

Neither of these papers, however, considers an alternative possibility that we had published (1), namely, that viral colonization of host genomes can account for apparent lateral transfer between distantly related organisms. This idea suggests that viruses can originate genes, then colonize either prokaryotes or eukaryotes to give the appearance of lateral gene transfer.

In prokaryotes, it is becoming increasingly clear that most genomic differences between groups are due to infectious events involving acquisition of new gene sets. We reported that the eukaryotic replication proteins appear to have been obtained from viral, not prokaryotic, sources because phycodnaviral DNA polymerase was phylogenetically ancestral to the replicative polymerase of eukaryotes. Because viruses (especially large DNA viruses) can persistently infect host prokaryotic and lower eukaryotic genomes and because they have an enormous capacity for creation of genetic novelty through recombination, viruses can explore more sequence space and at a more rapid rate than their cellular hosts. In figure 2 of their report, Salzberg *et al*. examine hyaluronan synthase as a possible example of lateral gene transfer. Although bootstrap values are not presented, the resulting phylogeny shows that the gene from phycodnavirus is basal to those found in vertebrates (but is still absent from lower eukaryotes). We suggest that this can support the idea that this gene originally colonized vertebrates from a virus.

Victor DeFilippis,[*]
Vaccine and Gene Therapy Institute,
Oregon Health Sciences University,
Beaverton, OR 97006, USA.

Luis P. Villarreal
Department of Molecular Biology and Biochemistry,
and Director, Center for Virus Research,
University of California,
Irvine, CA 92697, USA

[*]To whom correspondence should be addressed. E-mail: defilipp@ohsu.edu

References and Notes

1. L. P. Villarreal, V. R. DeFilippis, *J. Virol*. **74**, 7079 (2000).

Response

DeFilippis and Villarreal raise an excellent point: Integration of viral DNA into the genomes of free-living organisms might explain the presence of atypical genes in many species. If related viral genes independently made their way into different genomes, this could lead to mistaken conclusions about lateral gene transfer. To explore this possibility, we searched all of the genes considered as possible bacteria-to-vertebrate lateral transfers (BVTs) against all viral genes from the public databases. No significant matches between BVTs and viral genes were found, and therefore we did not have anything to report in our original study. We did find significant viral matches for some of the possible BVTs proposed in (1). Of the many phylogenetic trees that provided evidence against lateral gene transfer, the one that we chose to show in our figure 2 was selected because of the presence of a viral homolog. To determine whether the hypothesis of DeFilippis and Villarreal is correct, many more viral genomes need to be sequenced.

Steven L. Salzberg,*
The Institute for Genomic Research,
Rockville, MD 20850, USA

Jonathan A. Eisen
The Institute for Genomic Research,
Rockville, MD 20850, USA

*To whom correspondence should be addressed. E-mail: salzberg@tigr.org

References and Notes

1. International Human Genome Sequencing Consortium, *Nature* **409**, 860 (2001).

THE EDITORS SUGGEST THE FOLLOWING RELATED RESOURCES ON *SCIENCE* SITES:

In *Science* Magazine

REPORTS:
Microbial Genes in the Human Genome: Lateral Transfer or Gene Loss?
Steven L. Salzberg, Owen White, Jeremy Peterson, and Jonathan A. Eisen
Science 8 June 2001: 1903-1906 **Abstract »** **Full Text »** **PDF »** **Supplemental Data »**

PERSPECTIVES:
GENOMICS:
Enhanced: Are There Bugs in Our Genome?
Jan O. Andersson, W. Ford Doolittle, and Camilla L. Nesbø
Science 8 June 2001: 1848-1850 **Summary »** **Full Text »**