

 HORIZONTAL GENE TRANSFER

Unclonable, that's what you are!

Computation analysis allied with experimental proof has been used to show that genes that are toxic to a new host fail to transfer by horizontal gene transfer (HGT).

Rotem Sorek and colleagues reasoned that cloning genes into a foreign host (*Escherichia coli*) using plasmid vectors is akin to HGT by conjugation. Microbial genome sequences are typically assembled from sequenced fragments that have been cloned in *E. coli*. Sequence stretches that cannot be cloned are closed by clone-independent

PCR-based 'finishing'. With this in mind, the authors examined the original genome sequence data sets for evidence of genes that could (cloned genes) or could not (uncloned genes) be transferred by HGT.

Using the original data from 79 complete microbial genome sequences, they mapped the positions of all the clones used to generate the completed genomes against annotated genes, excluding genes larger than 1.5 kilobases. Some 'uncloned' loci were not represented in plasmid multicopy libraries, and a quarter of

these (124 genes) were absent from fosmid low-copy libraries, indicating that the unclonability of many genes is copy-number independent.

Of 61 loci that were uncloned from more than 5 genomes, half were present in single copies. These uncloned genes were mainly ribosomal structure and translation genes. When 39 of these uncloned genes were expressed in *E. coli* using an inducible expression vector, the *E. coli* cells died, indicating that the gene products were toxic. Computational analysis revealed that the genes that were tagged as unclonable in *E. coli* are predicted to be transfer-resistant throughout bacteria and archaea.

Toxicity to the host therefore seems to inhibit gene transfer, and this toxicity might be attributable to gene dosage. Understanding these limitations to HGT could have important implications for the choice of genes used to construct accurate phylogenetic trees.

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ORIGINAL RESEARCH PAPER Sorek, R. *et al.*
Genome-wide experimental determination of
barriers to horizontal gene transfer. *Science*
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