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New Evidence Suggests Genes in Parasites Were Acquired From Bacteria

<u>FOR IMMEDIATE RELEASE</u>

Genetic scientists studying a group of disease-causing parasites have identified 12 genes that appear to have been acquired from bacteria. Some of the genes enable the parasites, called nematodes, to attack and damage their hosts, said Dr. David Bird, study director and associate director of the Center for the Biology of Nematode Parasitism at North Carolina State University.

The study is the first to compare fully sequenced genomes to identify genes that have migrated "horizontally" from one species to another, in this case from soil bacteria to root-knot nematodes that infest plants. Identifying and targeting the genes responsible for parasitism may one day yield effective measures to combat these costly and disabling diseases.

The study, described in a paper published on May 19 in *Genome Biology*, is funded by a $2.6 million grant from the National Science Foundation and was performed in collaboration with scientists at NC State's Bioinformatics Research Center and at Washington University.

Nematodes are the largest and most destructive group of animals in the world. Billions of people, companion animals, and livestock suffer debilitating diseases caused by hookworm, roundworm, heartworm, and other nematodes. Plant-parasitic nematodes cause an estimated $100 billion a year in crop damage worldwide.

The findings also have significant implications for understanding the evolution of species, in which gene transfer from one species to another appears to play an important role.

Bird and his colleagues examined the genomes of three species of the root-knot nematode *Meloidogyne*, which deforms the roots of many crops including tobacco and tomato. The nematodes "hijack the plant's developmental pathways and form a feeding site in the roots, inhibiting the plant's growth," said Bird.

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"What makes the parasitic nematodes different from the free-living nematodes that do not harm plants and animals? This is the question scientists want to answer," said Bird. "The differences must be explained by their genes."

Bird and his colleagues developed two "phylogenetic filters," or computer methods of comparing genetic codes of different species. One filter found genes in the root-knot nematodes that were present in bacteria but were not present in the model non-parasitic nematode *C. elegans* or in fruit flies, which share an evolutionary ancestor with nematodes. The genes that passed through the first phylogenetic filter were then compared to a comprehensive genetic database of proteins to eliminate any other animal genes.

The 12 genes that passed through both phylogenetic filters had best matches to bacterial genes and were identified as candidates for horizontal gene transfer from bacteria. "This is a surprisingly large number of genes," said Bird.

Six of the 12 genes had been suggested by other researchers as possibly originating from bacteria, based on analysis of single genes or other evidence, and six were newly identified based solely on the genomic comparisons performed by Bird's group.

Seven of the candidate genes of bacterial origin are associated with enzymes that degrade cell walls or deform cell structure. "We started with no preconceived notions of the biological role of any transferred genes, so to have found mainly genes that have an apparent role in parasitism – that was a real surprise," said Elizabeth H. Scholl, an NC State doctoral student who helped design and implement the genomic comparisons.

Four of the candidate genes in the root-knot nematodes most closely matched genes in a group of nitrogen-fixing soil bacteria called rhizobia, which also live in and deform the roots of plants, but with beneficial rather than harmful effects. One match was to the rhizobial NodL gene, which is associated with formation of root nodules and was previously thought only to reside in rhizobia. These genes appear to have been transferred from the soil bacteria to presumably once-harmless nematodes, creating new species of parasites.

Bird hypothesizes that the acquisition of genes from bacteria was a key event in the evolution of nematode species. The first step was probably a symbiotic, or physically close and mutually beneficial, relationship between nematodes and bacteria, as is the case between certain bacteria living in nematodes that cause human diseases, such as elephantiasis and river blindness.

Bird is designing further experiments to verify horizontal gene transfer in nematodes and to identify which genes may be promising targets for developing disease-control methods.

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Note to editors: The abstract of the *Genome Biology* paper follows.

"Horizontally transferred genes in plant-parasitic nematodes: A high-throughput genomic approach"

Authors: Elizabeth H. Scholl, Jeffrey Thorne, David McK. Bird, North Carolina State University; James McCarter, Washington University and Divergence, Inc.
Date: Published in the May 19 edition of *Genome Biology*

Abstract: Published accounts of horizontally acquired genes in plant-parasitic nematodes have not been the result of a specific search for gene transfer per se, but rather have emerged from characterization of individual genes. We present a method for a high-throughput genome screen for horizontally acquired genes, illustrated using expressed sequence tag (EST) data from three species of root-knot nematode, *Meloidogyne spp.* Our approach identified the previously postulated horizontally transferred genes and revealed six new candidates. Screening was partially dependent upon sequence quality, with more candidates identified from clustered sequences than from raw EST data. Computational and experimental methods verified the horizontal gene transfer candidates as bona fide nematode genes. Phylogenetic analysis implicated rhizobial ancestors as donors of horizontally acquired genes in *Meloidogyne*. High-throughput genomic screening is an effective way to identify horizontal gene transfer candidates. Transferred genes that have undergone amelioration of nucleotide composition and codon bias have been identified using this approach. Analysis of these horizontally transferred gene candidates suggests a link between horizontally transferred genes in *Meloidogyne* and parasitism.