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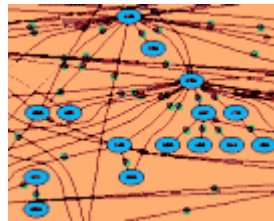
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### Fused genes give clues to deeper meaning

2 July 2001 18:00 EST

by *Apoorva Mandavilli*, [BioMedNet News](#)

Genes that are found separately in one genome are likely to be functionally related if they are fused together as a continuous sequence in another genome, announce researchers from Boston University. The results, published tomorrow in *Proceedings of the National Academy of Sciences*,

suggest that fusion-link analysis can be used to rapidly deduce the function of newly discovered genes and help elucidate pathways of gene regulation.

Although the idea that fused genes are functionally related has been described in the literature before, the reports were mostly "anecdotal," said Charles DeLisi, chairman of the bioinformatics program at Boston University and the principal investigator. "This is a systematic study of fused genes. We've constructed a very complex functional database."

New genes are being discovered in rapid numbers but many are of unknown function and do not have sequence homologs. Fusion-link analysis offers a method to pinpoint the function of a particular gene without using sequence correlation. Because of the scale of genomic information, it is important to carry out larger-scale, systematic analyses, rather than the anecdotal hypotheses published so far, DeLisi said, adding that fusion link analysis gives high-throughput results.

The researchers looked at genes from 30 microbial genomes and assigned each protein a functional category such as DNA replication, recombination, or signal transduction. Of the 4,515 fusion links they considered, they found that genes that are fused belong to the same functional category 72% of the time.

The results suggest that genes found separately in one genome are functionally related if they are fused together in another. Conversely, the investigators suggest, there is a high probability that an uncharacterized gene belongs to the same functional category as its fusion-link partner.

David Eisenberg and his colleagues at the University of California in Los Angeles first published the hypothesis that genes that are fused together are functionally related in 1999.

"I'm glad to see the method extended and used on a wide variety of genomes," said Eisenberg, director of the UCLA-DOE laboratory of structural biology and molecular medicine. The discovery of new genes is "marching ahead" and when that information is available, he said, "the tool will be much more

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*Current Opinion in Structural Biology*, Volume 10, Issue 3, 1 June 2000, 359-365

useful than it is now."

In his research, Eisenberg used fusion-link analysis, which he referred to as the "Rosetta stone method" and three others. He believes that when the tools are used together, they are even more powerful for understanding the function of a protein. A second method looks at the "phylogenetic profile" of proteins, in which functional interaction may be indicated if two proteins co-occur in genomes consistently. The other two tools look at spatial arrangement of genes and similarities in mRNA expression patterns.

"The most interesting part comes now," said Itai Yanai, a graduate student in DeLisi's lab and the lead author on the paper, adding that he plans to add genomes of *C. elegans*, *Arabidopsis*, *Drosophila* and the human genome to the fusion-link analysis.

"If you look at this web of interactions, you map and superimpose where the transcription factors and other genes involved in regulation are, you could get a lot of functional information about the genome," he said.

By studying which genes are functionally related, he explained, it may be possible to elucidate how genes are regulated. Those studies are now in progress and will likely be submitted for publication this summer.

"To me, the bottomline of such work is that the meaning of the function of a protein has now changed," said Eisenberg. A protein's function used to be defined by its action on a substrate or its binding to another molecule. Now, much as humans are defined by their interaction to others within society, he told *BioMedNet News*, "the function of a protein is the context of its interactions with other proteins in a cell."

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David Eisenberg,  
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Ioannis Xenarios, *et al.*  
*Nature*, 405, 823-826 (2000)

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Marcotte EM, Pellegrini M,  
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