Evaluating evolutionary rates could shed light into functions of uncharacterized genes

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Genes that have roles in the same biological pathways change their rate of evolution in parallel, a finding that could be used to discover their functions, said a researcher at the University of Pittsburgh School of Medicine in the February issue of *Genetics*.

Humans have nearly 21,000 genes that make as many proteins, but the functions of most of those genes have not been fully determined, said lead investigator Nathan Clark, Ph.D., assistant professor of computational and systems biology at the Pitt School of Medicine. Knowing what a particular gene does could help unravel the workings of the body, foster understanding of disease processes and identify targets for new drugs.

"For our study, we took a close look at the way genes evolved between species and we found an interesting signature," he said. "Genes that perform biological functions together have similar evolutionary histories in that the rates at which they change parallel each other. This could allow us to identify partner genes that we might never have suspected to work together in biochemical pathways."

The researchers studied the evolving genomes of 18 yeast species and 22 mammalian species, looking particularly at genes that are involved in meiosis, a cell division process, and in DNA repair. They found parallel changes, such as acceleration or deceleration, in evolutionary rates among not only genes encoding proteins that physically interact with each other, but also among those that had no direct contact but still

participated in meiosis or DNA repair pathways.

All genes mutate over time, which can be beneficial, harmful or meaningless. Some yeast species evolved a different method of reproduction and meiosis stopped as it was no longer essential for survival, Dr. Clark said. Through subsequent generations, the rate of change in the genes involved in making meiosis proteins accelerated, leading to deterioration of the unnecessary DNA sequences.

"A key question is: How important is that gene at that time?" he said. "If a species encounters a new challenge in its environment, the genes associated with it might have to evolve through subsequent generations in order to adapt that important pathway and ensure species survival."

By tracking those complementary rate changes, it could be possible to identify which genes participate in the same important pathways, providing clues to their function.

"In the future, a researcher studying a particular disease process might be able to plug in a couple of known genes in a database of evolutionary rate changes to find others that have a parallel history," Dr. Clark said. "That could provide new insight into the workings of the biological pathway of interest."

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