

# Researchers study evolution on the molecular level

December 13 2013, by Gary Galluzzo

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The theory of evolution suggests that present-day organisms evolved from earlier life forms.

At the molecular level, evolution reshaped some of the enzymes that help complete chemical processes—such as converting food into energy—in humans and all other life forms.

Now a University of Iowa researcher and his colleagues describe the evolution of various forms of the enzyme "dihydrofolate reductase" as it occurred from bacteria to humans. Their paper, "Preservation of Protein Dynamics in Dihydrofolate Reductase Evolution," appears in the Dec. 13 issue of the *Journal of Biological Chemistry*.

Amnon Kohen, professor of chemistry in the UI College of Liberal Arts and Sciences and member of the Interdisciplinary Program in Molecular and Cellular Biology, and his collaborators used bioinformatics (genetic sequencing information), computer-based calculations, artificial mutagenesis (DNA modification), and kinetic measurements in their work. They studied "humanized" forms of an enzyme that originated with the common bacterium *E. coli* in order to relate the action of [protein dynamics](#) and catalysis to the process of enzyme evolution.

They found that enzyme dynamics evolved over millions of years to optimize a specific catalyzed reaction that occurs in humans.

"Enzymes are critical components of every living cell, and they catalyze

almost all chemical reaction in life. We study how evolution occurred on the molecular level," Kohen says. "This study is an attempt to understand how evolution of the whole organism (for example from bacteria like *E. coli* to humans) is expressed on the [molecular level](#).

"We chose a 'housekeeping' enzyme, which is present in almost all organisms and is critical to life. That enzyme is called dihydrofolate reductase and is involved in DNA biosynthesis and all cells' replication," he says.

He says the researchers "bridged" between the bacterial and human enzymes by producing 'humanized' [bacterial enzyme](#), meaning modifying parts of the bacterial enzyme to have the amino-acids sequence of the human enzyme. This was done based on a comparison of enzyme sequences of many organisms ranging from bacteria to human.

"We found that while many steps in the catalytic cascade of these enzymes are evolving, the actual chemical conversion catalyzed by the enzymes is conserved along evolution—meaning that even in the bacteria, the enzyme already has perfectly oriented the reactants in its active site, as well as in the human enzyme. This outcome was not expected, as the human enzyme is much faster and quite different genetically," he says.

Kohen says that the study is significant in that it shows that the dynamics of enzyme evolution is preserved along evolution from bacteria to humans.

"The finding significantly affects how the scientific community understands what was important for evolutionary pressure to preserve and what is unimportant," he says. "For example, the preservation of enzyme dynamics that are involved in catalyzing the chemical conversion are very fast and were not expected to play a role in evolution, thus our

findings will bring researchers to consider such fast dynamics not only in evolution, but also in the design of drugs used against this enzyme (and maybe enzymes in general) or the design of bio-mimetic (nature inspired) catalysts."

Kohen says that his study of the diverging genetic sequences between *E. coli* and Homo sapiens illustrates the process of evolution at a basic level.

"We start with *E. coli* because it is at a basic level, and we use bioinformatics to trace the [evolution](#) of a single [enzyme](#)," he says.

Provided by University of Iowa

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