Resurrection of extinct enzymes reveals evolutionary strategy for the invention of new functions

December 11 2012

How does evolution innovate? We exist because our ancestors have had the ability to adapt successfully to changes in their environment; however, merely examining present-day organisms can limit our understanding of the actual evolutionary processes because the crucial events have been masked by the passage of aeons – what we need is a time machine. Scientists from VIB, KU Leuven, University of Ghent and Harvard have done the next-best thing; by reconstructing DNA and proteins from prehistoric yeast cells, they were able to directly examine the evolutionary forces that have acted over the last 100 million years to shape modern-day enzymes – biological catalysts that enable organisms to manipulate molecules to their will.

The scientists set out to explore how new genes emerge, how they contribute to the survival of the evolving organism, and how, after a humble start, evolution then refines the function of new genes and hones the efficiency of the enzymes that they encode. One of the richest sources of such new genes is the chance duplication of existing genes. One copy of the gene can then continue to encode the original enzyme, allowing it to perform its original task, while the other is free to change and to perhaps take on a new function; alternatively, the two new enzymes might sub-divide the original task.

Although this pattern of innovation is known to have happened many thousands of times during evolution, the way in which it occurs hasn't

been clear. In a paper published December 11 in the online Open Access journal PLOS Biology, Karin Voordeckers, Chris Brown and Kevin Verstrepen from VIB in Leuven, together with Steven Maere from VIB and the University of Ghent, tackled this problem, focusing their attention on the evolution of enzymes that have allowed yeast to exploit changing food sources over the last 100 million years of evolution.

The scientists 'resuscitated' ancestral yeast genes, allowing them to examine the properties of enzymes that existed tens of millions of years ago. The original enzyme originally enabled the yeast cells to survive on a diet of maltose, a common sugar, but duplications of their genes gave rise to new enzymes which opened up the possibility of feeding off other types of sugar in the environment. The resurrection of these enzymes meant that the scientist could build up a detailed picture of their atomic structure and directly determine their ability to break down different types of sugars. Armed with this information, they could work out exactly how the enzymes had changed their specificity and how evolution drove their optimisation.

"We used sequence reconstruction algorithms to predict the DNA sequence of ancestral genes from dozens of present-day DNA sequences. This enabled us to rebuild the corresponding ancestral proteins and compare them with those present today", said Steven Maere.

"We searched very specifically for how the yeast adapted to break down various sources of sugar. We found that the primal gene that codes for the protein for the digestion of maltose – a sugar in grain – was copied a number of times during evolution. The DNA of some copies changed slightly, resulting in new proteins that could break down different sugars. By modeling these changes in the corresponding proteins, we now understand how just a few changes in the DNA can lead to the development of a completely new activity in the corresponding proteins", said Karin Voordeckers.

"New functional DNA does not appear out of thin air, but is built up gradually from a copy of an existing segment of functional DNA. By reconstructing a piece of prehistoric DNA that was copied several times during evolution, we were able to investigate in detail which changes occur in each of the copies and gradually lead to new functions. As such, our results provide a unique and detailed view into the molecular details of Darwinian evolution" says Kevin Verstrepen.

The scientists propose that the events observed here in the yeast cell's quest for sugar may reflect a general strategy widely used for innovation in evolution.

More information: Voordeckers K, Brown CA, Vanneste K, van der Zande E, Voet A, et al. (2012) Reconstruction of Ancestral Metabolic Enzymes Reveals Molecular Mechanisms Underlying Evolutionary Innovation through Gene Duplication. PLOS Biol 10(12): e1001446. doi:10.1371/journal.pbio.1001446