

When Silent Mutations Provide Evolutionary Advantages

Until recently, most biologists believed that so-called silent mutations, created by 'synonymous' DNA changes—those that do not affect the protein-coding sequence—had very weak effects on the evolution of organisms.

However, a new study by an international team of scientists has shown that a different set of DNA codes specifying the same product can have major effects on the survival and evolution of bacteria. Moreover, they have now shown that single highly beneficial synonymous mutations can allow organisms to rapidly evolve and adapt to their environment.

Working on the bacterium *Methylobacterium extorquens*, the group created several variants of a gene called *fae*, a metabolic enzyme essential for survival and growth in an environment where the only source of carbon comes from methanol or methylamine. Under such restrictive conditions, bacteria undergo strong selection for retaining the *fae* gene function. When grown in conditions where methanol was provided as the sole carbon source, all bacterial populations with the "synonymous" *fae* gene variants performed poorly when compared with bacteria carrying the normal gene.

However, when bacterial populations carrying these variants of *fae* were grown over a long period of time with methanol being the only carbon source—described as "strong selection conditions," an interesting phenomenon was observed. Within 100–200 generations, these bacterial populations began to regain their fitness through additional mutations to the gene variants. Many of these mutations

were again synonymous. Furthermore, these mutations occurred at single points within the gene, were highly beneficial, and they seemed to recur in multiple experiments.

"What is surprising about our results is that the beneficial mutations we see are highly repeatable in specific gene variants—you can think of this process with an analogy to climbers—different climbers who start independently from the bottom of a hill are using the exact same strategy to reach the top," said Agashe, from the National Centre for Biological Sciences, Bangalore, and lead author of the publication, published in the early online edition of the journal *Molecular Biology and Evolution*. The new study is not only critical to understanding the genetic basis of adaptation, but also, the development of antibiotic resistance.

Reference

Agashe D, Sane M, Phalnikar K, Diwan GD, Habibullah A, Martinez-Gomez NC, Sahasrabuddhe V, Polacheck W, Wang J, Chubiz LM, et al. 2016. Large-effect beneficial synonymous mutations mediate rapid and parallel adaptation in a bacterium. *Mol Biol Evol* 33:1542–1553.

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doi:10.1093/molbev/msw078

Advance Access publication May 2, 2016

Adaptation Helps Fish Thrive in Toxic Environments

An extremophile fish—the small, Atlantic molly—can live in caves and springs throughout Mexico and thrive in water so toxic that most forms of life die within minutes.

Now, a 10-year collaborative project led by biologists Kelley et al. (2016) has shown how the fish can survive in toxic, hydrogen sulfide waters.

"Learning how these extremophiles function tells us something very fundamental about life itself," said corresponding author Michael Tobler, Kansas State University assistant professor of biology. "We are able to learn about the boundaries where life can exist, which tells us something basic about how cells and organisms work."

Using genomic tools, the researchers compared gene expression of the mollies living in toxic hydrogen sulfide environments with others living in nontoxic environments. The scientists found that about 170 of the fish's 35,000 or so genes were turned on, or upregulated, to detoxify and remove the hydrogen sulfide.

They found that the fish have a two-pronged approach to survival. They become inert to the toxins that enter the body and are able to detoxify hydrogen sulfide more efficiently. The poison invades the fishes' bodies, but their proteins can help the fish break down the hydrogen sulfide into nontoxic forms and excrete it.

Hydrogen sulfide shuts down energy production in cells by interfering with specific proteins. The fish combat this challenge by using anaerobic metabolism, which is an alternative—although much less efficient—way to produce energy and does not involve oxygen.

"It's not that they're keeping the hydrogen sulfide out," said Kelley, a genome scientist at Washington State University. "It's not that they are necessarily turning on some other unrelated genes. It's really that the genes that have been previously implicated in hydrogen sulfide detoxification are turned on or turned up. That's really the exciting part."