# Context crucial when it comes to mutations in genetic evolution, study reports

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With mutations, it turns out that context can be everything in determining whether or not they are beneficial to their evolutionary fate.

According to the traditional view among biologists, a central tenet of evolutionary biology has been that the evolutionary fates of new mutations depend on whether their effects are good, bad or inconsequential with respect to reproductive success. Central to this view is that "good" mutations are always good and lead to reproductive success, while "bad" mutations are always bad and will be quickly weeded out of the gene pool.

However, new research led by evolutionary biologist Jay Storz of the University of Nebraska-Lincoln has found that whether a given mutation is good or bad is often determined by other mutations associated with it. In other words, genetic evolution is context-dependent.

In a study to be published in the June 14 issue of *Science*, Storz and colleagues at UNL and Aarhus University in Denmark report that an individual mutation can be beneficial if it occurs in combination with certain other mutations, but the same mutation can detrimental to the organism if it occurs in other combinations.

The researchers studied mutations that alter the function of hemoglobin, the protein in charge of transporting oxygen in the blood. Physiologists have long known that many high-altitude animals have evolved hemoglobins with high affinities for oxygen, which can enhance oxygen uptake in thin air. Earlier research by Storz's group on populations of North American deer mice that are native to high and low altitudes had found that the high-altitude mice had evolved hemoglobins with an increased oxygen-binding affinity—and that this difference is attributable to the combined effects of genetic mutations at 12 different sites in the hemoglobin protein.

For the discovery reported in *Science*, the researchers used a technique called "protein engineering" to synthesize hemoglobin proteins that contained each of the naturally occurring mutations in all possible multi-site combinations.

"By measuring the oxygen-binding properties of these engineered hemoglobins, we discovered that the same individual mutations produced an increased oxygen-affinity in some combinations and they produced a decreased oxygen-affinity in other combinations. Their effects are completely context-dependent," said Storz, an associate professor of biological sciences.

"One of the important implications is that if there are interactions between mutations, then some mutational pathways of evolution may be more accessible than others. The evolutionary fate of a new mutation will depend critically on which other mutations have already occurred. The order in which mutations occur can determine whether evolution is more likely to follow some pathways rather than others. Evolution may follow certain pathways just because certain interactions may be negative, other interactions may be positive. These kinds of interaction effects determine what mutational pathways are open and available for evolution."

**More information:** "Epistasis Among Adaptive Mutations in Deer Mouse Hemoglobin," by C. Natarajan et al. *Science*, 2013.

Provided by University of Nebraska-Lincoln